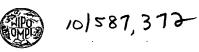
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(54) Title: DNA SEQUENCES AND PLASMIDS FOR CONCENTRATION	THE	PREPARATION OF SUGAR BEET WITH CHANGED SUCROSE
(57) Abstract		
DNA sequences and plasmids are described, that by in	ntegrati	on in a plant genome of sugar beet change the sucrose concentration, as
well as transgenic plants that by introduction of the DNA se	equence	es of the invention causes changes in sugar concentration.
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Title: <u>DNA sequences and plasmids for the preparation of</u> sugar beet with changed sucrose concentration

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Field of the invention

The present invention relates to DNA sequences and plasmids, containing these DNA sequences, which by integration into the genome of a sugar-beet plant, changes the sugar metabolism of the plant to be changed. The invention also relates to transgenic plants formed with the help of these sequences.

Sucrose is of central importance for the plant and serves many functions. For the long distance transport of 15 photoassimilates and/or energy between various organs in plants, sucrose is almost exclusively used. The sucrose, which is transported in a specific heterotrophic organ, determines the growth and the development of this organ. Thus it is known, e.g. from EP 442 592, that transgenic 20 plants, in which the transport away of the sucrose from the exporting leaves is inhibited by expression of an apoplastic invertase, shows a strong reduction in the growth of e.g. roots or tubers in the case of potato plants. For tobacco plants, the principal importance of 25 sucrose as the central function for the long distance transport of energy carriers within the plant is described (von Schaewen et al, 1990, EMBO J 9: 3033-3044).

Further it is also known from EP 455 316 that DNA sequences present on plasmids, after introduction in a plant genome of a potato plant can affect the starch biosynthesis as well altering the amount and composition of the protein in the potato tubers.

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Whilst it has known that a reduction of the amount of sucrose imported in the heterotrophic organs, such as tubers and seeds, leads to loss of yield, it is not known whether an increase in the amount of sucrose in the photosynthetically active parts of the plant, mainly the leaves, leads to a better supply of heterotrophic organs and thus to an increase in yield.

Besides sucrose and/or the hexoses, glucose and fructose,
derived from sucrose, have the property of protection of
plants against frost damage at low temperatures. Frost
damage is one of the main limiting factors in agricultural
productivity in the northern hemisphere. Temperatures
below freezing lead to the formation of ice crystals.

Since the growing ice crystals consist of pure water,
water is abstracted from the cells as the temperature

This dehydration has at least two potential damaging 20 results:

falls.

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- All dissolved substances within a cell are strongly concentrated and the cell contracts following the loss of water. Highly concentrated salts and organic acids lead to membrane damage.
- 2. With rehydration from dew, the previously contacted cells reexpand. The cell membrane also expands again. The volume expansion puts a heavy mechanical load on the membrane.
- It is thus clear that a freezing/dew cycle can lead to severe membrane damage of the cells and thus to damage to the plant.
- 35 It thus appears worth trying to hinder the freezing. One

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possible strategy is the increased formation of osmotically active substances in the cytosol of plant cells. This should lead to a lowering of the freezing point. Osmotically active substances include sucrose and/or the two hexoses derived from sucrose.

The increased formation of sucrose and/or the two hexoses at low temperatures is desirable in the growing plant.

Another situation can exist in the harvested parts of a plant, especially in storage.

In relation to the economic aspects, sucrose thus possesses two especially important functions:

- as the transport form for the distant transport of photoassimilates,
- as an osmotically active substance with the desirable activity of lowering the freezing point in intact, growing plants.
- The biosynthesis pathways for the formation of sucrose, either from the primary photosynthesis products (in the leaf) or by breakdown of starch (in the storage organs e.g. of potatoes), are known.
- It is however, not known how and in what way changes of the carbohydrate concentration in sugar beet can be achieved since it is not possible to use even very similar genes such as for example genes that code for a sucrose synthase, ADP-glucose pyrophosphorylase or sucrose phosphate synthase of the potato with satisfactory success for the preparation of sugar beet with changed sucrose concentration. An exact analysis and determination of the DNA sequences or sequence fragments for the sugar beet is thus required.

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To change the sugar concentration in sugar beet, DNA sequences are now provided which code for the small and large subunit of the ADP glucose pyrophosphorylase, the sucrose synthase and the sucrose phosphate synthase of sugar beet (Seq. ID No 1-4).

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These DNA sequences can be introduced into plasmids and in this way combined with steering elements for expression in eukaryotic cells. Such steering elements are on the one hand transcription promoters and on the other hand transcription terminators. Each plasmid comprises:

- a) a suitable promoter which ensures that the coding sequence meets a suitable time point or in the specified developments in the transgenic plant or in determined genes of transgenic plants;
- b) at least a coding sequence for sugar beet that

 i) is so coupled to the promoter that the

 formation of an RNA is allowed which is into a

 protein, whereby the protein demonstrates an

 enzymatic activity which leads to a change of

 the sucrose concentration in the plant, or
 - ii) which is so coupled to the promoter that the coding part is read, which leads to the formation of a so-called anti-sense RNA which under-expresses the formation of the protein coded from an endogenous gene in the plant, that is involved in the sucrose biosynthesis; and
 - c) A non-coding termination sequence that contains the signal for the termination and polyadenylation of the transcript.

The coding sequences named under b) are the sequences that code for the large and small subunit of the ADP glucose pyrophosphorylase, for the sucrose phosphate synthase and for the sucrose synthase of sugar beet.

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The large subunit of the ADP-glucose-pyrophosphorylase has the following nucleotide sequence (Seq. ID No. 1):

CAAAAGAAAA ACTTCCCATT TCTACTTCTT TGCACAATAT AATTTCCCAC	0050
CAATTTTCT TTAAATTTCT CACTTTCATT TAATCAGTTT TCAGCAACAT	0100
TCTGATACTC GACAACCCAC TTTCTGTTCT CCCAAGATTC CAAACCTCTG	0150
ATTCTCATTC CACTAATATT TTTGCTTATT TTTTTTCTGG ATTTAAAGAA	0200
AAGCT ATG GAT GCA AGT GCA GCA GCC ATA AAT GTC AAT GCC CAT Met Asp Ala Ser Ala Ala Ala Ile Asn Val Asn Ala His 5 10	0243
TTA ACA GAA GTT GGA AAG AAA CGT TTT TTA GGA GAG AGA ATC AGT	0288
Leu Thr Glu Val Gly Lys Lys Arg Phe Leu Gly Glu Arg Ile Ser	
15 20 25	
CAA AGT TTG AAG GGT AAA GAT CTG AGA GCT CTG TTT TCA AGA ACT	0333
Gln Ser Leu Lys Gly Lys Asp Leu Arg Ala Leu Phe Ser Arg Thr	
30 35 40	
GAG AGC AAG GGT AGA AAT GTC AAT AAA CCT GGG GTT GCA TTT TCT	0378
Glu Ser Lys Gly Arg Asn Val Asn Lys Pro Gly Val Ala Phe Ser	
45 50 55	
GTT CTC ACC TCA GAT TTT AAT CAA AGT GTT AAA GAA TCT TTG AAA	0423
Val Leu Thr Ser Asp Phe Asn Gln Ser Val Lys Glu Ser Leu Lys	
60 65 70	

TAT	GAG	CCA	GCA	TTA	TTT	GAA	TCT	CCA	AAA	GCT	GAC	CCA	AAA	AAT	0468
Tyr	Glu	Pro	Ala	Leu	Phe	Glu	Ser	Pro	Lys	Ala	Asp	Pro	Lys	Asn	
	75					80					85			•	
GTG	GCT	GCA	ATT	GTG	CTG	GGT	GGT	GGT	GCT	GGG	ACT	CGC	CTC	TTT	0513
Val	Ala	Ala	Ile	Val	Leu	Gly	Gly	Gly	Ala	Gly	Thr	Arg	Leu	Phe	
	90					95					100				
CCT	CTT	ACT	AGC	AGG	AGA	GCT	AAG	CCA	GCA	GTG	CCA	ATT	GGA	GGG	0558
Pro	Leu	Thr	Ser	Arg	Arg	Ala	Lys	Pro	Ala	Val	Pro	Ile	Gly	Gly	
	105					110					115				
TGT	TAC	AGG	CTG	ATT	GAT	GTG	CCT	ATG	AGC	AAC	TGC	ATC	AAC	AGT	0603
Суѕ	Tyr	Arg	Leu	Ile	Asp	Val	Pro	Met	Ser	Asn	Cys	Ile	Asn	Ser	
	120					125					130				
			AAG												0648
Gly	Ile	Arg	Lys	Ile	Phe	Ile	Leu	Thr	Gln	Phe	Asn	Ser	Phe	Ser	
	135					140	•				145				
														GTG	0693
Leu	Asn	Arg	His	Leu	Ala	Arg	Thr	Tyr	Asn	Phe	Gly	Asp	Gly	Val	
	150					155					160				
														ACA	0738
Asn	Phe	Gly	Asp	Gly	Phe	Val	Glu	Val	Phe	Ala	Ala	Thr	Gln	Thr	
	165					170					175				

CCT	GGA	GAA	TCA	GGA	AAG	AAA	TGG	TTC	CAG	GGC	ACC	GCT	GAT	GCA	0783
Pro	Gly	Glu	Ser	Gly	Lys	Lys	Trp	Phe	Gln	Gly	Thr	Ala	Asp	Ala	
	180					185					190			•	
GTA	AGA	CAG	TTT	TTC	TGG	GCA	TTT	GAG	GAT	TCC	AAA	TCC	AAG	GAT	0828
Val	Arg	Gln	Phe	Phe	Trp	Ala	Phe	Glu	Asp	Ser	Lys	Ser	Lys	Asp	
	195					200					205				
GTC	GAG	CAT	ATA	GTT	ATT	TTA	TCC	GGT	GAT	CAT	CTT	TAC	CGA	ATG	0873
Val	Glu	His	Ile	Val	Ile	Leu	Ser	Gly	Asp	His	Leu	Tyr	Arg	Met	
	210					215					220				
		ATG													0918
Asp	_	Met	Ser	Phe	Trp		Lys	His	Ile	Asp		Asn	Ala	Asp	
	225					230					235				
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		Val													0,000
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	240														
TAT	GGG	CTG	ATG	AAG	ATT	GAT	CAC	ACT	GGA	CGC	ATT	GTC	CAT	TTT	1008
		Leu													
-1-	255			-4 -		260					265				
GCA	GAA	AAA	ccc	AAG	GGT	TCT	GAT	CTA	ACA	GCA	ATG	CAA	GTA	GAT	1053
Ala	Glu	Lys	Pro	Lys	Gly	Ser	Asp	Leu	Thr	Ala	Met	Gln	Val	Asp	
	270					275					280				

									GAA						1098
Thr	Thr	Val	Leu	Gly	Leu	Ser	Asp	Leu	Glu	Ala	Met	Ser	Asn	Pro	
	285					290					295			•	
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TAT	ATT	GCA	TCA	ATG	GGT	GTT	TAT	GTC	TTT	CGA	ACG	GAT	GTT	CTT	1143
									Phe						
	300					305					310				
ATG	GAG	CTT	CTC	AAT	CGA	AAA	TAC	CCT	TCA	AGC	AAT	GAT	TTT	GGC	1188
									Ser						
	315					320	_				325				
	310														
40 C40	GAG	Aጥጥ	ATT	CCT	TCA	GCT	GTA	GGA	GAG	TCT	AAT	GTT	CAG	GCA	1233
									Glu						
001	330					335		-			340				
TAT	CTA	ттт	AAT	GAC	TAC	TGG	GAG	GAT	ATC	GGA	ACC	ATA	AAG	TCT	1278
									ATC Ile						1278
	Leu								ATC Ile						1278
						Trp					Thr				1278
Tyr	Leu 345	Phe	Asn	Asp	Tyr	Trp 350	Glu	Asp	Ile	Gly	Thr 355	Ile	Lys	Ser	1276
Tyr	Leu 345 TTT	Phe GAT	Asn TCC	Asp AAT	Tyr TTG	Trp 350 GCC	Glu CTT	Asp ACA	Ile	Gly CAG	Thr 355 CCT	Ile	Lys AAG	Ser TTT	
Tyr	Leu 345 TTT Phe	Phe GAT	Asn TCC	Asp AAT	Tyr TTG	Trp 350 GCC Ala	Glu CTT	Asp ACA	Ile	Gly CAG	Thr 355 CCT	Ile	Lys AAG	Ser TTT	
Tyr	Leu 345 TTT	Phe GAT	Asn TCC	Asp AAT	Tyr TTG	Trp 350 GCC	Glu CTT	Asp ACA	Ile	Gly CAG	Thr 355 CCT Pro	Ile	Lys AAG	Ser TTT	
Tyr	Leu 345 TTT Phe	Phe GAT	Asn TCC	Asp AAT	Tyr TTG	Trp 350 GCC Ala	Glu CTT	Asp ACA	Ile	Gly CAG	Thr 355 CCT Pro	Ile	Lys AAG	Ser TTT	
Tyr TTC Phe	Leu 345 TTT Phe 360	Phe GAT Asp	Asn TCC Ser	Asp AAT Asn	Tyr TTG Leu	Trp 350 GCC Ala 365	Glu CTT Leu	Asp ACA Thr	Ile CAA Gln	Gly CAG Gln	Thr 355 CCT Pro 370	Ile CCC Pro	Lys AAG Lys	Ser TTT Phe	
TYr TTC Phe	Leu 345 TTT Phe 360	Phe GAT Asp	TCC Ser	Asp AAT Asn	TYT TTG Leu	Trp 350 GCC Ala 365	CTT Leu	Asp ACA Thr	CAA Gln	CAG Gln ACA	Thr 355 CCT Pro 370	CCC Pro	Lys AAG Lys	TTT Phe	1323
TYr TTC Phe	Leu 345 TTT Phe 360	Phe GAT Asp	TCC Ser	Asp AAT Asn	TYT TTG Leu	Trp 350 GCC Ala 365	CTT Leu	Asp ACA Thr	Ile CAA Gln	CAG Gln ACA	Thr 355 CCT Pro 370	CCC Pro	Lys AAG Lys	TTT Phe	1323

CTG	CCT	CCT	ACA	AAA	GTC	GAC	AGG	TGC	AAG	ATT	GTC	GAT	TCC	ATT	1413
Leu	Pro	Pro	Thr	Lys	Val	Asp	Arg	Cys	Lys	Ile	Val	Asp	Ser	Ile	
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											ATC				1458
vaı		HIS	GIY	cys	Pne		GIN	GIU	ser	Ser	Ile	GIN	Hls	Ser	
	405					410					415				
ATT	GTT	GGT	GTT	CGC	TCA	AGA	TTA	GAG	TCC	GGG	GTT	GAG	TTC	CAG	1503
Ile	Val	Gly	Val	Arg	Ser	Arg	Leu	Glu	Ser	Gly	Val	Glu	Phe	Gln	
	420					425					430				
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														GAA	1348
Asp		Met	Mec	Met	GIY	440	Asp	Tyr	Tyr	GIN	Thr 445	GIU	ser	GIU	
	435	-				440					443				
ATT	GCT	TCT	CTG	CTT	GCT	GAG-	GGA	AAG	GTT	CCT	GTT	GGT	GTC	GGA	1593
Ile	Ala	Ser	Leu	Leu	Ala	Glu	Gly	Lys	Val	Pro	Val	Gly	Val	Gly	
	450					455					460				
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	407										4,5				
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Ile	Gly	Lys	Asp	Val	Val	Ile	Ala	Asn	Thr	Asp	Gly	Val	Glu	Glu	
	400					125					400				

GCA	GAT	AGA	CCA	AAT	GAA	GGC	TTT	TAC	ATC	AGG	TCG	GGC	ATT	ACC	1728
Ala	Asp	Arg	Pro	Asn	Glu	Gly	Phe	Tyr	Ile	Arg	Ser	Gly	Ile	Thr	
	495					500					505			•	
ATC	ΑͲͲ	TTG	AAG	AAC	GCA	ACC	ATA	CAA	GAC	GGT	CTT	GTG	ATT	TAG	1773
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CTC	GCA	TTC	TCC	TCT	TCT	TCT	CTC	TCC	GGC	GAC	AAA	ATT	CAA	ACG	0089
Leu	Ala	Phe	Ser	Ser	Ser	Ser	Leu	Ser	Gly	Asp	Lys	Ile	Gln	Thr	
15					20					25					
						•									
ACG	TCA	TTT	CTC	AAC	CGC	CGA	TAT	TGT	AGA	ATC	TCT	TCT	AGA	GCT	0134
Thr	Ser	Phe	Leu	Asn	Arg	Arg	Tyr	Cys	Arg	Ile	Ser	Ser	Arg	Ala	
					35					40					

CCG	ATT	GTT	GTC	TCT	CCC	AAA	GCT	GTT	TCT	GAT	TCT	AAG	AAT	TCG	0179
Pro	Ile	Val	Val	Ser	Pro	Lys	Ala	Val	Ser	Asp	Ser	Lys	Asn	Ser	
45					50					55					
CAG	ACT	TGT	CTT	GAC	CCT	GAA	GCC	AGC	CGT	AGT	GTT	CTT	GGT	ATT	0224
Gln	Thr	Cys	Leu	Asp	Pro	Glu	Ala	Ser	Arg	Ser	Val	Leu	Gly	Ile	
60					65					70					
ATA	CTT	GGA	GGT	GGT	GCT	GGT	ACA	CGT	CTT	TAC	CCG	TTG	ACT	AAG	0269
Ile	Leu	Gly	Gly	Gly	Ala	Gly	Thr	Arg	Leu	Tyr	Pro	Leu	Thr	Lys	
75					80					85					
												•			
AAG	AGA	GCC	AAA	CCA	GCC	GTG	CCA	CTC	GGT	GCT	AAT	TAT	AGG	CTT	0314
Lys	Arg	Ala	Lys	Pro	Ala	Val	Pro	Leu	Gly	Ala	Asn	Tyr	Arg	Leu	
90					95					100					
TTA	GAT	ATC	CCA	GTG	AGC	TAA	TGT	TTG	AAC	AGT	AAT	ATT	TCC	AAA	0359
Ile	Asp	Ile	Pro	Val	Ser	Asn	Cys	Leu	Asn	Ser	Asn	Ile	Ser	Lys	
105					110					110					
ATA	TAT	GTT	CTT	ACA	CAA	TTC	AAT	TCT	GCT	TCT	CTG	AAT	CGT	CAT	0404
Ile	Tyr	Val	Leu	Thr	Gln	Phe	Asn	Ser	Ala	Ser	Leu	Asn	Arg	His	
115					120					125					
										GGA					0449
	Ser	Arg	Ala			Ser	Asn	Met	Gly	Gly	Tyr	Lys	Asn	Glu	
130					135	•				140					
										AGT					0494
_	Phe	Val	Glu	Val		Ala	Ala	Gln		Ser	Pro	Glu	Asn	Pro	
145					150					155					

AAC	TGG	TTT	CAG	GGT	ACA	GCT	GAT	GCT	GTT	AGG	CAA	TAT	CTG	TGG	0539
Asn	Trp	Phe	Gln	Gly	Thr	Ala	Asp	Ala	Val	Arg	Gln	Tyr	Leu	Trp	
160					165					170					
CTT	TTC	GAA	GAG	CAC	AAT	GTT	CTT	GAG	TAC	TTG	ATT	CTT	GCT	GGT	0584
Leu	Phe	Glu	Glu	His	Asn	Val	Leu	Glu	Tyr	Leu	Ile	Leu	Ala	Gly	
175					180					185					
		•													
GAC	CAT	TTG	TAT	CGA	ATG	GAT	TAT	GAA	AGA	TTT	GTC	CAA	GCT	CAC	0629
Asp	His	Leu	Tyr	Arg	Met	Asp	Tyr	Glu	Arg	Phe	Val	Gln	Ala	His	
190					195					200					
			٠.												
										GCA					0674
_	Glu	Thr	Asp	Ala		Ile	Thr	Val	Ala	Ala	Leu	Pro	Met	Asp	
205					210					215					
C 3 3	7 7 C	CCT	CCM	a cm	CCA	ատա	GGT	ጥጥር	እጥር	AAA	ያ ጥጥ	CAT	CAA	CAA	0719
										Lys					0,13
220	Буб	AL 9	VIG	1111	225	1110	011	ДСС		230		p	014	O14	
220					223										
GGA	AGA	ATT	ATT	GAG	TTT	GCC	GAG	AAA	CCG	AAA	GGA	GAA	CAA	TTG	0764
										Lys					
235					240			_		245	_				
						•									
AAA	GCT	ATG	AAG	GTT	GAT	ACC	ACA	ATC	CTG	GGT	CTG	GAC	GAT	GAG	0809
Lys	Ala	Met	Lys	Val	Asp	Thr	Thr	Ile	Leu	Gly	Leu	qzA	qzA	Glu	
250					255					260					

PCT/EP94/01671

AGA	GCA	AAA	GAA	ATG	CCA	TTC	ATA	GCC	AGC	ATG	GGC	ATA	TAT	GTT	0854
Arg	Ala	Lys	Glu	Met	Pro	Phe	Ile	Ala	Ser	Met	Gly	Ile	Tyr	Val	
265					270					275					
										CGG					0899
Ile	Ser	Lys	Asp	Val	Met	Leu	Asn	Leu	Leu	Arg	Glu	Gln	Phe	Pro	
280					285					290					
										CCA					0944
-	Ala	Asn	Asp	Phe	_	Ser	Glu	Val	Ile	Pro	Gly	Ala	Thr	Ser	
295					300					305					
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		mm.c		<b>c</b> mo	033	CCM	mam	mmc	mam	C N M	C C M	m > C		CNC	0000
										GAT					0989
	GIY	Leu	Arg	val	315	Ala	TYL	Leu	ıyı	Asp 320	GIY	IÀT	пр	GIU	
310					313					320					
GAT	ATT	GGT	ACC	ATT	GAA	GCT	TTT	TAC	AAT	GCT	AAC	TTG	GGA	ATC	1034
										Ala					
325		•			330			-		335			-		
ACC	AAA	AAG	CCG	GTG	CCA	GAT	TTT	AGC	TTC	TAT	GAT	CGT	TCA	TCT	1079
Thr	Lys	Lys	Pro	Val	Pro	Asp	Phe	Ser	Phe	Tyr	Asp	Arg	Ser	Ser	
340					345					350					
CCA	ATT	$\mathtt{TAT}$	ACA	CAA	CCT	CGG	TAT	TTG	CCT	CCT	TCA	AAG	ATG	CTT	1124
Pro	Ile	Tyr	Thr	Gln	Pro	Arg	Tyr	Leu	Pro	Pro	Ser	Lys	Met	Leu	
355					360					365					

GAT	GCT	GAT	ATA	ACT	GAC	AGC	GTC	ATC	GGT	GAA	GGC	TGT	GTT	ATT	1169
Asp	Ala	Asp	Ile	Thr	Asp	Ser	Val	Ile	Gly	Glu	Gly	Cys	Val	Ile	
370					375					380					
AAG	AAC	TGT	AAG	ATT	CAT	CAT	TCT	GTT	ATC	GGA	CTT	CGA	TCT	TGT	1214
Lys	Asn	Cys	Lys	Ile	His	His	Ser	Val	Ile	Gly	Leu	Arg	Ser	Cys	
385		•	-		390					395		-			
ATC	TCG	GAG	GGT	GCA	ATC	ATT	GAG	GAC	ACA	CTG	TTG	ATG	GGA	GCT	1259
										Leu					
400			-		405			_		410			_		
GAT	TAT	TAT	GAG	ACT	GAT	GCT	GAT	CGG	AAA	TTC	CTG	GCT	GCT	AAG	1304
										Phe					
415	-	-			420					425					
GGT	AGT	GTA	CCT	ATT	GGA	ATT	GGG	AAT	GCA	CGT	ATT	GGG	GAT	GAT	1349
Gly	Ser	Val	Pro	Ile	Gly	Ile	Gly	Asn	Ala	Arg	Ile	Gly	Asp	Asp	
430					435					440				••	
GTC	AAG	ATT	ATC	AAC	AGT	GAC	AAT	GTA	CAA	GAA	GCA	GCA	AGA	GAA	1394
Val	Lys	Ile	Ile	Asn	Ser	Asp	Asn	Val	Gln	Glu	Ala	Ala	Arg	Glu	
445	-				450					455					
ACA	C3.C	GGA	TAC	TTC	ATA	AAG	AGC	GGA	ATA	GTC	ACT	ATA	ATC	AAG	1439
	GAC														
						Lys	Ser	Gly	Ile	Val	Thr	Ile	Ile	Lys	
						Lys	Ser	Gly	Ile	Val 470	Thr	Ile	Ile	Lys	
Thr					Ile	Lys	Ser	Gly	Ile		Thr	Ile	Ile	Lys	

Asp		ATG	ATT	CCA	AGT	GGA	ACT	GTA	ATC	TAG	AAA'	TGGA	GCA		1482
_	Ala	Met	Ile	Pro	Ser	Gly	Thr	Val	Ile	End					
475					480					485				•	
					•										
TAT	AATA	AAT A	ATCA	CTGC	CT A	ATTI	CAGT	CC.	ratc:	rgag	TCT	CCCA	CCA		1532
TGA	CCCT	rtg 2	ATTC	AATC	rt ti	ragt:	ratgi	LAA 1	ATAT	TTTT	GGC'	TTTT	GCG		1582
ATT	TTGC	CAT A	AAAT	TGA	AG A	AGCG/	AGGAT	TC	AGGG	ACGA	TAG	rgct:	ATG		1632
AAT	rggaz	AGA A	AAGG <i>I</i>	ATTTO	G GC	GAT	ATCTI	TG	ΓΑΑΑΊ	GACA	TTT	rgac'	TAC		1682
												•			
TGG	GCAC:	CAA A	AAATI	rtggi	ra an	rgcT?	ATACO	: AA	ATA!	CATA	AAA	AGAT	CTT		1732
GCT	GGT:	TTT (	GTA.	LAAA	AA AA	KAAA/	AAAA	A							1763
	The	suc	crose	pho	spha	ate -	- syr	thas	se ha	as th	ne fo	ollo	wing		
	nuc	cleot	-ide	sent	ience	100	.~ T	D M							
				209	761166	: (36	=y• 4	או ע.	). J	<b>:</b>					
			-140	Sequ	161166	: (36	sy. ı	או ע.	). J	):					
GGG			SAAGO								AAT	GAT			0044
GGG								ATG	GCG						0044
GGG								ATG	GCG	GGA				·	0044
GGG								ATG	GCG	GGA		Asp			0044
	CTGC?	AGG (	GAAGO	CTCTC	GA AC	CTTC!	AAAA	ATG Met	GCG Ala	GGA Gly	Asn	Asp 5	CCA	GGA	0044
TGG	CTGC?	AGG (	GAAGO	TAT	GA AC	CTTC!	LAAA GCA	ATG Met ATT	GCG Ala CTG	GGA Gly GAT	Asn GTG	Asp 5 GGT			
TGG	CTGC?	AGG (	GAAGO AGT	TAT	GA AC	CTTC!	LAAA GCA	ATG Met ATT	GCG Ala CTG	GGA Gly GAT	Asn GTG	Asp 5 GGT			
TGG	CTGC?	AGG (	GAAGO AGT	TAT Tyr	GA AC	CTTC!	LAAA GCA	ATG Met ATT	GCG Ala CTG Leu	GGA Gly GAT	Asn GTG	Asp 5 GGT		Gly	
TGG Trp	ATA	AGG ( AAC Asn	GAAGO AGT Ser	TAT Tyr 10	GA AC TTA Leu	CTTCA GAG Glu	GCA Ala	ATG Met ATT Ile	GCG Ala CTG Leu 15	GGA Gly GAT Asp	Asn GTG Val	Asp 5 GGT Gly	Pro	Gly 20	
TGG Trp CTT	ATA Ile GAT	AGG ( AAC Asn GAT	AGT Ser GCA	TAT Tyr 10	TTA Leu TCA	GAG Glu TCT	GCA Ala	ATG Met ATT Ile	GCG Ala CTG Leu 15	GGA Gly GAT Asp	Asn GTG Val	Asp 5 GGT Gly AGA	Pro GGC	Gly 20 AGG	0089
TGG Trp CTT	ATA Ile GAT	AGG ( AAC Asn GAT	GAAGO AGT Ser	TAT Tyr 10	TTA Leu TCA	GAG Glu TCT	GCA Ala	ATG Met ATT Ile	GCG Ala CTG Leu 15	GGA Gly GAT Asp	Asn GTG Val	Asp 5 GGT Gly AGA	Pro GGC	Gly 20 AGG	0089
TGG Trp CTT	ATA Ile GAT	AGG ( AAC Asn GAT	AGT Ser GCA	TAT Tyr 10 AAA Lys	TTA Leu TCA	GAG Glu TCT	GCA Ala	ATG Met ATT Ile	GCG Ala CTG Leu 15 TTG Leu	GGA Gly GAT Asp	Asn GTG Val	Asp 5 GGT Gly AGA	Pro GGC	Gly 20 AGG	0089
TGG Trp CTT Leu	ATA Ile GAT Asp	AAC Asn GAT Asp	AGT Ser GCA Ala	TAT Tyr 10 AAA Lys 25	TTA Leu TCA Ser	GAG Glu TCT Ser	GCA Ala TTG Leu	ATG Met ATT Ile CTT Leu	GCG Ala CTG Leu 15 TTG Leu 30	GGA Gly GAT Asp AGA	GTG Val GAA Glu	Asp 5 GGT Gly AGA Arg	Pro GGC Gly	Gly 20 AGG Arg 35	0089
TGG Trp CTT Leu	ATA Ile GAT Asp	AAC Asn GAT Asp	AGT Ser GCA Ala	TAT Tyr 10 AAA Lys 25	TTA Leu TCA Ser	GAG Glu TCT Ser	GCA Ala TTG Leu	ATG Met ATT Ile CTT Leu	GCG Ala CTG Leu 15 TTG Leu 30	GGA Gly GAT Asp AGA Arg	Asn GTG Val GAA Glu	Asp 5 GGT Gly AGA Arg	Pro GGC Gly GGT	Gly 20 AGG Arg 35	0089
TGG Trp CTT Leu	ATA Ile GAT Asp	AAC Asn GAT Asp	AGT Ser GCA Ala	TAT Tyr 10 AAA Lys 25	TTA Leu TCA Ser	GAG Glu TCT Ser	GCA Ala TTG Leu	ATG Met ATT Ile CTT Leu	GCG Ala CTG Leu 15 TTG Leu 30	GGA Gly GAT Asp AGA Arg	Asn GTG Val GAA Glu	Asp 5 GGT Gly AGA Arg	Pro GGC Gly GGT	Gly 20 AGG Arg 35	0089

GAT	GAA	ACC	GAC	CTT	CAT	CGT	TCA	TGG	GTT	CGG	GCA	CAA	GCA	ACA	0224
Asp	Glu	Thr	Asp	Leu	His	Arg	Ser	Trp	Val	Arg	Ala	Gln	Ala	Thr	
				55					60					65	
										GAG					0269
Arg	Ser	Pro	Gln		Arg	Asn	Thr	Arg		Glu	Asn	Met	Cys	Trp	
				70					75					80	
AGA	ATT	TGG	AAT	TTG	GCT	CGT	CAG	AAG	AAG	CAG	CTT	GAG	AAT	GAA	0314
Arg	Ile	Trp	Asn	Leu	Ala	Arg	Gln	Lys	Lys	Gln	Leu	Glu	Asn	Glu	
_		_		85					90					95	
GAA	GCT	CAG	CGG	AAG	ACA	AAA	CGT	CGT	ATG	GAG	CTT	GAG	AGG	GGT	0359
Glu	Ala	Gln	Arg	Lys	Thr	Lys	Arg	Arg	Met	Glu	Leu	Glu	Arg	Gly	
				100					105	•	•			110	
CGT	CGA	GAA	GCA	ACT	GCT	GAT	ATG	TCG	GAG	GAC	TTA	TCA	GAA	GGC	0404
Arg	Arg	Glu	Ala	Thr	Ala	Asp	Met	Ser	Glu	Asp	Leu	Ser	Glu	Gly	
•	_			115					120					125	
										ACC					0449
Glu	Lys	Asp	Ile		Ala	His	Gly	Asp		Thr	Arg	Pro			
				130					135					140	
CCA	AGA	АТА	AAT	TCT	CTT	GAT	GCT	ATG	GAG	ACA	TGG	ATT	AGT	CAA	0494
Pro	Arg	Ile	Asn	Ser	Leu	Asp	Ala	Met	Glu	Thr	Trp	Ile	Ser	Gln	
				145					150					155	
						•									
					<b>c</b> mc	m» c	C C C C C C C C C C C C C C C C C C C	cmm	mm.c	3003	3 C M	omm.	C D M	CCM	0520
										ATA					0539
Gln	Lys	GIU	гÀг		ьeu	Tyr	ren			Ile	ser	ьeи			
				160					165				•	170	

TTG	ATA	CGA	GGT	GAA	AAC	ATG	GAA	CTT	GGC	CGT	GAT	TCT	GAT	ACT	0584
Leu	Ile	Arg	Gly	Glu	Asn	Met	Glu	Leu	Gly	Arg	Asp	Ser	Asp	Thr	
				175					180					185	
GGT	GGT	CAG	GTT	AAG	TAT	GTG	GTT	GAG	CTT	GCA	AGG	GCT	CTA	GGT	0629
Gly	Gly	Gln	Val	Lys	Tyr	Val	Val	Glu	Leu	Ala	Arg	Ala	Leu	Gly	
				190					195					200	
												•			
TCG	ATG	CCA	GGT	GTT	TAT	AGA	GTT	GAT	TTG	CTA	ACT	AGG	CAA	GTT	0674
Ser	Met	Pro	Gly	Val	Tyr	Arg	Val	Asp	Leu	Leu	Thr	Arg	Gln	Val	
				205					210					215	
TCA	TCT	CCT	GAC	GTG	GAT	TGG	AGT	TAT	GGG	GAG	CCT	ACT	GAG	ATG	0719
Ser	Ser	Pro	Asp	Val	Asp	Trp	Ser	Tyr	Gly	Glu	Pro	Thr	Glu	Met	
				220					225					230	
CTG	AAT	CCA	AGG	GAT	TCC	AAT	GGT	TTT	GAT	GAT	GAT	GAT	GAT	GAA	0764
Leu	Asn	Pro	Arg	Asp	Ser	Asn	Gly	Phe	Asp	Asp	Asp	Asp	Asp	Glu	
				235					240					245	
									GTT				TTT		0809
									GTT Val				TTT		0809
													TTT Phe		0809
				Ser					Val				TTT Phe	Gly	0809
Met	Gly	Glu	Ser	Ser 250	Gly	Ala	Tyr	Ile	Val 255	Arg	Ile	Pro	TTT Phe	Gly 260	
Met	Gly AGG	Glu GAT	Ser AAG	Ser 250	Gly ATC	Ala	Tyr AAA	Ile GAA	Val 255 GAG	Arg	Ile TGG	Pro	TTT Phe	Gly 260 ATT	0809
Met	Gly AGG	Glu GAT	Ser AAG	Ser 250	Gly ATC	Ala	Tyr AAA	Ile GAA	Val 255	Arg	Ile TGG	Pro	TTT Phe TAT	Gly 260 ATT Ile	
Met	Gly AGG	Glu GAT	Ser AAG	Ser 250	Gly ATC	Ala	Tyr AAA	Ile GAA	Val 255 GAG	Arg	Ile TGG	Pro	TTT Phe TAT	Gly 260 ATT	

CCL	GAA	TTT	GTT	GAI	GGI	GCI	CIA	AAC	CAC	NIN	GII	CAA	AIG	100	0099
Pro	Glu	Phe	Val	Asp	Gly	Ala	Leu	Asn	His	Ile	Val	Gln	Met	Ser	
				280					285					290	
AAA	GTT	TTA	GGT	GAG	CAA	ATT	GGT.	AGC	GGG	GAA	ACA	GTT	TGG	CCA	0944
									Gly						
_1 -		_	-	295			_		300					305	
GTT	GCC	АТТ	CAT	GGA	CAT	TAT	GCT	GAT	GCT	GGT	GAT	TCT	GCT	GCT	0989
									Ala						
141				310		-1-			315					320	
				323											
ىلىلى	СТТ	тст	GGT	GGC	СТА	AAT	GTT	CCA	ATG	CTT	TTA	ACG	GGG	CAT	1034
									Met						
БСС	Dea	001	011	325		•••			330					335	
ייריי יי	Ctrtr	GGC	CGA	GAC	AAG	TTA	GAG	CAG	CTC	CTC	AAA	CAG	GGT	CGA	1079
									Leu						
DCI	Dea	CLI	9	340	-1-				345		•			350	
				340					• • •						
እጥር	ጥርጥ	ΔΔΔ	САТ	GAC	АТА	AAC	ААТ	ACA	TAC	AAA	ATA	ATG	CGT	AGG	1124
									Tyr						
Mec	261	БУЗ	пор	355					360	-1-				365	
				333					,,,,					• • •	
አጥአ	CNN	GCC	GAA	GAG	ጥጥA	'тса	СТТ	GAT	GCC	тст	GAG	ATA	GTC	АТА	1169
									Ala						
TTE	GIU	WIG	GIU		neu	JEI	שבע	vah	375	DCI	JIU			380	
				370					د ، د					200	

ACT	AGI	ACA	AGA	CAA	GAA	ATA	GAA	GAG	CAA	TGG	CAC	CTC	TAT	GAT	1214
Thr	Ser	Thr	Arg	Gln	Glu	Ile	Glu	Glu	Gln	Trp	His	Leu	Tyr	Asp	
				385					390					395	
GGG	TTT	GAT	CCT	GTG	CTA	GAA	CGT	AAA	CTC	CGT	GCT	AGG	ATG	AAG	1259
Gly	Phe	Asp	Pro	Val	Leu	Glu	Arg	Lys	Leu	Arg	Ala	Arg	Met	Lys	
				400					405	_				410	
								٠							
CGT	GGT	GTA	AGC	TGT	TAT	GGA	AGG	TTC	ATG	ccc	CGG	ATG	GTT	GTT	1304
										Pro					
5	1			415	-,-	2	5		420		,			425	
ATT	CCT	CCT	GGA	ATG	GAA	TTC	AAT	CAT	ATT	GTT	CCA	CAT	GAG	GGT	1349
										Val					
			2	430					435					440	
				•••											
GAT	ATG	GAT	GGT	GAA	ACA	GAA	GAA	ACT	GAA	GAG	CAT	ССТ	ACA	TCA	1394
										Glu					
			2	445					450					455	
сст	GAT	CCA	ССТ	ATC	TGG	GCT	GAG	ATT	ATG	CGC	TTC	TTT	TCT	AAA	1439
										Arg					
				460					465	5				-1- 470	
CCA	AGG	AAG	CCA	ATG	ATA	CTT	GCC	СТТ	GCT	AGG	ССТ	GAC	CCG	AAG	1484
										Arg					-101
110	nr 9	יבעה		475					480	9		p		485	
				4,5					700					-05	

AAG	AAT	ATC	ACG	ACT	TTG	GTC	AAA	GCA	T"I"I	GGA	GAA	TGC	CGT	CCA	1529
Lys	Asn	Ile	Thr	Thr	Leu	Val	Lys	Ala	Phe	Gly	Glu	Cys	Arg	Pro	
				490					495					500	
СТА	AGG	GAG	CTA	GCT	AAT	CTT	ACT	CTT	ATA	ATG	GGT	AAC	CGA	GAT	1574
		Glu													
	5			505					510		-		_	515	
сст	ΑΤΤ	GAC	GAG	ATG	TCA	AGC	ACC	AGT	TCT	TCA	GTT	CTC	CTG	TCA	1619
		Asp													
O ₁	110			520					525					530	
				•••											
GTG.	СФФ	AAG	СТА	ልጥጥ	GAT	CAA	TAC	GAC	СТТ	TAT	GGT	CAA	GTA	GCA	1664
		Lys													
Val	Пеп	כעם	Dea	535		<b>02</b>	-1-		540	-,-	1			545	
				<b>93</b> 3					• • • • • • • • • • • • • • • • • • • •						
መእር	ccc	AAA	יעעט.	CAC	AAG	C & A	ССТ	GAT	СТТ	ССТ	GAG	ATT	ТАТ	CGT	1709
		Lys													
TYL	PIO	гì	ura	550	БУЗ	GIII	nia	nsp	555	110	014	-1-0		600	
				550										000	
		GCA	220	202	7 7 C	CCA	CTC	ጥጥጥ	ን መመ	חממ	CCA	CCT	עיעיעי	ערים ע	1754
															1/54
Leu	Ala	Ala	гÀг		гÀг	GIĀ	vai	Pne		ASII	PIO	Ald			
				605					610					615	
						·		<b></b>	201	603	C OM	0.m	CCIII	mm »	1700
		TTT													1799
Glu	Pro	Phe	Gly		Thr	Leu	TIE	GIU		ATS	ΑТЯ	nis			
				620					625					630	

CCG	ATG	GII	GCT	ACG	AAA	AAT	GGA	GGC	CCT	G.L.I.	GAT	ATC	CAG	AGG	1844
Pro	Met	Val	Ala	Thr	Lys	Asn	Gly	Gly	Pro	Val	Asp	Ile	Gln	Arg	
				635					640					645	
GTC	CTT	GAT	ААТ	GGT	CTT	CTT	GTG	GAT	CCT	CAT	GAG	CAG	CAG	TCT	1889
Val	Leu	Asp	Asn	Gly	Leu	Leu	Val	Asp	Pro	His	Glu	Gln	Gln	Ser	
		_		650				_	655					660	
ATT	GCT	ACT	GCT	TTG	CTG	AAG	СТТ	GTT	GCT	GAT	AAG	CAA	СТА	TGG	1934
											Lys				
				665		•			670	•	•			675	
ACA	AAA	TGC	CAG	CAA	AAT	GGA	CTG	AAA	AAT	ATT	CAT	CTC	TAC	TCT	1979
											His				
	•	•		680		-		•	685				-	690	
TGG	CCA	GAG	CAT	TCG	AAG	ACA	TAC	CTA	TCT	CGA	ATA	GCC.	AGT	TCG	2024
Trp	Pro	Glu	His	Ser	Lys	Thr	Tyr	Leu	Ser	Arg	Ile	Ala	Ser	Ser	
				695	•		•		700	,				705	
AGA	CAA	AGG	CAA	CCA	CAG	TGG	CAA	AGA	AGT	AGT	GAT	GAA	GGG	CTT	2069
											Asp				
9		9		710					715					720	
GAC	TAA	CAA	GAG	ССТ	GAA	TCT	CCA	AGT	GAT	тст	TTA	AGA	GAT	ATA	2114
											Leu				
p	AJII	O ±11		725					730			7		735	

AAG	GAT	ATA	TCT	CTA	AAC	CTT	GAA	GTT	CTC	GTT	AGA	CCG	GAG	AAA	2159
Lys	Asp	Ile	Ser	Leu	Asn	Leu	Glu	Val	Leu	Val	Arg	Pro	Glu	Lys	
				740					745					750	
AGG	GTG	AAG	ACG	TTG	AAA	ATC	TTG	·GGA	TTG	ATG	ACA	AAA	GCA	TAA	2204
Arg	Val	Lys	Thr	Leu	Lys	Ile	Leu	Gly	Leu	Met	Thr	Lys	Ala	Asn	
				755					760					765	
TCG	AGA	ATG	CTG	TTA	TGT	TCA	TGG	TCT	AAT	GGT	GTC	CAT	AAG	ATG	2249
Ser	Arg	Met	Leu	Leu	Cys	Ser	Trp	Ser	Asn	Gly	Val	His	Lys	Met	
				770					775					780	
CTT	CGG	AAG	GCT	CGG	TTC	TCT	GAC	AAA	GTA	GAT	CAG	GCT	TCT	AGT	2294
Leu	Arg	Lys	Ala	Arg	Phe	Ser	Asp	Lys	Val	Asp	Gin	Aic	Ser	Ser	
				785					790					795	
									CTT						2339
Lys	Tyr	Pro	Ala		Arg	Arg	Arg	Lys	Leu	Ile	Tyr	Val			
				800					805					810	
									TTT						2384
Val	Asp	Gly	Asp		GIU	Asp	GIÀ	Leu	Phe	Asp	TIE	Val			
				815					820					825	
											٠				
		<b>~</b> 3~		~ ~ ~	~~~	220	C 3 C		3 CC	<i>a</i> , ,	~~~	mcc.	N	666	2422
									ATT						2429
Ile	Phe	Asp	Ala	Ala	GTÄ	ьys	GIU	ьys	Ile	GTA	GIA	ser	TTG	GIA	

$\mathbf{T}\mathbf{T}\mathbf{T}$	ATA	TTG	TCA	ACA	TCC	TAT	TCT	ATG	CCC	GAA	ATT	CAG	AAC	TAT	2474
Phe	Ile	Leu	Ser	Thr	Ser	Tyr	Ser	Met	Pro	Glu	Ile	Gln	Asn	Tyr	
				845					850					855	
TTG	CTA	TCA	AAA	GGC	TTC	AAT	CTT	CAT	GAT	TTT	GAT	GCA	TAT	ATA	2519
Leu	Leu	Ser	Lys	Gly	Phe	Asn	Leu	His	Asp	Phe	Asp	Ala	Tyr	Ile	
			_	860					865					870	
TGC	AAC	AGT	GGG	AGT	GAG	TTG	TAC	TAT	TCA	TCT	TTG	AAC	TCA	GAG	2564
												Asn		_	
-2 -				875			•	•	880					885	
GAG	AGT	AAT	ATT	АТА	GCA	GAT	TCA	GAT	TAC	CAT	TCA	CAC	ATA	GAG	2609
												His			
				890		•		-	895					900	
TAC	AGA	TGG	GGT	GGA	GAA	GGC	CTT	AGA	AGG	ACT	TTG	CTT	CGC	TGG	2654
												Leu			
		•	•	905		•		_	910					915	
GCA	GCT	TCC	ATC	ACA	GAA	AAA	AAT	GGT	GAA	AAC	GAA	GAA	CAG	GTT	2699
												Glu			
	-	•		920		•		•	925					930	
ATT	ACT	GAA	GAT	GAA	GAA	GTT	тст	ACG	GGT	TAT	TGC	TTT	GCG	TTT	2744
												Phe			
			E	935					940	4	<b>4</b> -			945	

AAA	ATA	AAG	AAC	CAA	AAT	AAG	GTT	CCC	CCT	ACG	AAG	GAG	CTC	CGC	2789
Lys	Ile	Lys	Asn	Gln	Asn	Lys	Val	Pro	Pro	Thr	Lys	Glu	Leu	Arg	
				950					955					960	
		ATG													2834
Lys	Ser	Met	Arg	Ile	Gln	Ala	Leu	Arg	Cys	His	Val	Ile	Tyr	Cys	
				965					970					975	
		GGA													2879
Gln	Asn	Gly	Ser	Lys	Met	Asn	Val	Ile		Val	Leu	Ala			
				980					985					990	
															2224
		GCC													2924
Ser	Gln	Ala	Leu		Tyr	Leu	Tyr			Trp	GIÀ	Val			
				995				1	.000				1	005	
mcc	* ~ ~	ATG	COUT	CTC	ጥጥጥ	CTT	CC A	GAA	முற்	сст	GAC	<b>2</b> C 2	GAT	ጥልጥ	2969
		Met													2505
ser	гуѕ	met			File	Val	GIY		.015	GIY	nsp	1111		020	
			L	1010				_	.013				_	020	
CDD	GGC	TTG	СТТ	GGC	GGG	GTC	CAT	AAA	ACC	GTA	ATA	CTG	AAG	GGA	3014
		Leu													
	CII			1025					.030					035	
•															
GTC	TCC	AAC	ACT	GCT	TTA	AGG	TCT	CTC	CAT	GCC	AAC	AGA	AGT	TAC	3059
Val	Ser	Asn	Thr	Ala	Leu	Arg	Ser	Leu	His	Ala	Asn	Arg	Ser	Tyr	
			1	1040				3.	045				3.	050	

CCT CTT TCA CAT GTC GTG TCG CTT GAC AGC CCC AAT ATT GGC GAG	3104
Pro Leu Ser His Val Val Ser Leu Asp Ser Pro Asn Ile Gly Glu	
1055 1060 1065	
GTG AGC AAA GGG TGC AGC AGC TCC GAG ATC CAG TCC ATC GTC ACA	3149
Val Ser Lys Gly Cys Ser Ser Ser Glu Ile Gln Ser Ile Val Thr	3149
1070 1075 1080	
20.0	
AAA CTC TCC AAA GCT TAA TCAGATATCT GCTGCTTTCT TTTGGGTAAG	3197
Lys Leu Ser Lys Ala End	
1085	
CAAGGTTTCA TCTTATATGA TTATATCATA AGATACTATA TAAGCACCTT	3247
AND	2207
ATTGGTAAGT CAGTCCCATA ATAATAATGT ACTTCAGAAC CACAATACTT	3297
AAAAGTTGGT TCAGTAGTGA TTAGTCTCAT AATAATCATA TAATTACACA	3347
AAAGIIGII ICIGIIGIGA EENTEETAA VANASAA AAAAAA	
TCCGCTGTTA ACTAGTGGTA ATATCTAAGC TCAACAATAA AGATGTAAAA	3397
TGCTAGTATG GAAATGAATT GCTAGCTGTT GATCTCTTTC CCTTTATTCT	3447
GTATTATTTC TTTCCTCATC TCATGTAAAA ACAATTTTCT GAAGGTGTAC	3497
	2545
AGTTTTTTCC CCTTATATAT CTGTATTATT TCTACTATTT TTTGTTTGTA	3547
AGAATATCCT CTCATCGAGG AGTGATAATT AAATAACCGG CTTGCTAAAT	3597
AGAATATUUT CTCATCGAGG AGIGATAATI AAATAACCGG CTIGCTAAAT	3377
ATAAAGCTTA TTCGAGTTAA AAAAAAAAA AAAAAAAA	3635

The sucrose-synthase has the following nucleotide sequence (Seq. ID No. 4):

CT	GCA	GGA	GGG	AAA	CAA	ATT	CTT	AGC	GAT	GGC	CCG	TTT	AGC	GAA	004
	Ala	Gly	Gly	Lys	Gln	Ile	Leu	Ser	Asp	Gly	Pro	Phe	Ser	Glu	
					5			•		10					
GTT	CTT	AGG	TCT	GCT	CAG	GAA	GCA	ATA	GTT	GTT	CCT	CCC	TTT	GTT	0089
Val	Leu	Arg	Ser	Ala	Gln	Glu	Ala	Ile	Val	Val	Pro	Pro	Phe	Val	
15					20					25			•		
GCT	ATA	GCA	GTC	CGT	CCA	AGA	CCT	GGA	GTT	TGG	GAA	TAT	GTT	CGT	0134
												Tyr			
30					35					40					
GTT	AAT	GTC	TCT	GAA	CTG	AAT	GTG	GAG	CAG	CTA	ACT	GTG	TCT	GAG	0179
Val	Asn	<b>Val</b>	Ser	Glu	Leu	Asn	Val	Glu	Gln	Leu	Thr	Val	Ser	Glu	
45					50					55					
TAT	CTC	CAT	TTC	AAG	GAA	GAA	CTT	GTG	GAT	GGA	AAG	GCT	GAT	GAC	0224
Tyr	Leu	His	Phe	Lys	Glu	Glu	Leu	Val	Asp	Gly	Lys	Ala	Asp	Asp	
60					65					70					
CAC	TAT	GTG	CTT	GAG	CTT	GAT	TTC	GAG	CCT	TTT	AAT	GAA	TCA	GTT	0269
His	Tyr	Val	Leu	Glu	Leu	Asp	Phe	Glu	Pro	Phe	Asn	Glu	Ser	Val	
75					80					85					
CCA	CGT	CCA	ACT	CGC	TCT	TCA	TCA	ATT	GGT	AAT	GGT	GTT	CAG	TTC	0314
Pro	Arg	Pro	Thr	Arg	Ser	Ser	Ser	Ile	Gly	Asn	Gly	Val	Gln	Phe	
90					95					100					
CTC	AAT	CGG	CAC	CTG	TCA	TCA	AGC	ATG	TTC	TGC	AAC	AAA	GAT	TGC	0359
Leu	Asn	Arg	His	Leu	Ser	Ser	Ser	Met	Phe	Cys	Asn	Lys	qzA	Cys	
105					110					115					

TTG	GAG	CCG	TTA	CTT	GAT	TTT	CTT	AGA	GTG	CAC	AAA	CAT	AAA	GGA	0404
Leu	Glu	Pro	Leu	Leu	Asp	Phe	Leu	Arg	Val	His	Lys	His	Lys	Gļy	
120					125					130					
GTT	GTC	ATG	ATG	TTG	AAT	GAT	CGG	ATA	CAG	ACT	ATC	CAG	CGT	CTT	0449
Val	Val	Met	Met	Leu	Asn	Asp	Arg	Ile	Gln	Thr	Ile	Gln	Arg	Leu	
135					140					145					
CAG	TCT	GCA	TTG	TCT	AAA	GCT	GAG	GAT	TAT	CTT	ATC	AAA	CTT	CCA	0494
Gln	Ser	Ala	Leu	Ser	Lys	Ala	Glu	Asp	Tyr	Leu	Ile	Lys	Leu	Pro	
150					155					160					
GCA	GAT	ACA	CCT	TAC	TCT	GAG	TTC	GAA	TTT	GTA	ATC	CAA	GGT	ATG	0539
Ala	Asp	Thr	Pro	Tyr	Ser	Glu	Phe	Glu	Phe	Val	lie	G) n	Gly	Met	
165					170					175					
GGT	TTT	GAA	AGA	GGC	TGG	GGT	GAT	ACT	GCT	GAA	AGG	GTT	CTA	GAA	0584
Gly	Phe	Glu	Arg	Gly	Trp	Gly	Asp	Thr	Ala	Glu	Arg	Val	Leu	Glu	
180					185					190					
										GCT					0629
	Met	His	Leu	Leu		Asp	Ile	Leu		Ala	Pro	Asp	Pro	Ser	
195					200					205					
														GTG	0674
	Leu	GIu	Thr	Phe		GIÀ	Arg	Leu		Met	val	Lue	Asn	val	
210					215			•		220					

GTC	ATT	TTG	TCT	GTA	CAT	GGA	TAT	TTT	GGA	CAG	GCA	CAT	GTG	CTC	0719
Val	Ile	Leu	Ser	Val	His	Gly	Tyr	Phe	Gly	Gln	Ala	His	Val	Leu	
225					230					235					
GGC	TTG	CCT	GAC	ACT	GGT	GGG	CAG	ΆΤΑ	GTT	TAT	ATA	CTT	GAC	CAA	0764
_										Tyr					
240			•		245	-				250			_		
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GTG	cee	тСт	CTG	GAA	CAT	GAA	ATG	CTC	CAA	CGA	ATA	AAG	AAG	CAA	0809
										Arg					
255	Arg	261	Leu	Gia	260	014			• • • • • • • • • • • • • • • • • • • •	265		-10	_,_		
233					200										
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ССТ	GAC	CCT	מממ	GGG	ACC	ACG:	TGC	A A T	CAA	CGT	ATG	GAG	AAA	GTC	0899
										Arg					
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285					230					2,5					
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a		CCR	N TIC	CTC	ccc	. א ת ת	TICC	מידית	TI CT	A C A	முரு	CAT	CTA	TGG	0989
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	Lys	Gly	Ile	Leu		Lys	Trp	TTE			Pne	Asp	vai	Trp	
Glu 315	Lys	Gly	Ile	Leu	Arg 320	Lys	Trp	TTE		Arg 325	Pne	Asp	Val	Trp	
	Lys	Gly	Ile	Leu		Lys	Trp	116			Pne	ASP	vai	Trp	

CCT	TAT	TTA	GAG	ACC	TTC	ACT	GAG	GAT	GCA	GCT	GGT	GAA	ATT	TTA	1034
Pro	Tyr	Leu	Glu	Thr	Phe	Thr	Glu	Asp	Ala	Ala	Gly	Glu	Ile	Ile	
330					335					340					
GGC	GAG	TTG	CAG	GGT	CGT	CCA	GAT	·CTG	ATA	ATT	GGC	AAC	TAC	AGC	1079
Gly	Glu	Leu	Gln	Gly	Arg	Pro	Asp	Leu	Ile	Ile	Gly	Asn	Tyr	Ser	
345					350					355					
GAT	GGG	AAT	ATA	GTT	GCT	TCT	TTA	TTG	TCC	CAC	AAA	ATG	GGT	GTC	1124
Asp	Gly	Asn	Ile	Val	Ala	Ser	Leu	Leu	Ser	His	Lys	Met	Gly	Val	
360					365					370					
ACC	CAG	TGC	AAT	ATA	GCC	CAT	GCA	TTG	GAG	AAA	ACC	AAG	TAT	CCA	1169
Thr	Gln	Cys	Asn	Ile	Ala	His	Ala	Leu	Glu	Lys	Thr	Lys	TYT	Pro	
375					380					385					
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										GAC					1214
-	Ser	Asp	Ile	Tyr	_	Lys	Arg	Phe	Glu	Asp	Lys	Tyr	His	Phe	
390					395					400					
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										ATG					1259
	Cys	GIN	Pne	ser		ASP	Leu	met		Met	ASN	HIS	Ala	Asp	
405					410					415					
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720					423					450					

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Thr	Val	Gly	Gln	Tyr	Glu	Ser	His	Lys			Thr	Phe	Pro	Gly	
435					440					445					
em a	m » m	000	cmc	CTUT	CAC	ccc	ያ ሙሙ	CAT	GTC.	ተጥተ	GAT	CCC	AAG	ጥጥጥ	1394
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Asn	Ile	Val	Ser	Pro	Gly	Ala	Asp	Met	Ala	Ile	Tyr	Phe	Pro	Phe	
465					470					475					
mc »	CAC	2 2 C	ርስጥ	GTC	ACC	ጥርጥ	СТС	АСТ	тса	СТТ	CAT	AGA	CTT	ATA	1484
											His				
	014					•				490					
480					485					400					
480										450					
GAG					AAA					GAA				GGT	1529
GAG					AAA Lys					GAA Glu	GAA Glu				1529
GAG					AAA					GAA					1529
GAG Glu					AAA Lys					GAA Glu					1529
GAG Glu 495	Gln	Leu	Leu	Phe	AAA Lys 500	Pro	Glu	Gln	Asn	GAA Glu 505	Glu	His	Ile	Gly	1529 1574
GAG Glu 495 GTA	Gln TTA	Leu	Leu	Phe	AAA Lys 500	Pro AAG	Glu	Gln	Asn ATA	GAA Glu 505	Glu	His ATG	Ile	Gly	
GAG Glu 495 GTA	Gln TTA	Leu	Leu	Phe	AAA Lys 500	Pro AAG	Glu	Gln	Asn ATA	GAA Glu 505	Glu	His ATG	Ile	Gly	
GAG Glu 495 GTA Val	Gln TTA	Leu	Leu	Phe	AAA Lys 500 TCA Ser	Pro AAG	Glu	Gln	Asn ATA	GAA Glu 505 TTT Phe	Glu	His ATG	Ile	Gly	
GAG Glu 495 GTA Val 510	Gln TTA Leu	Leu GAT Asp	Leu GAT Asp	Phe ACC Thr	AAA Lys 500 TCA Ser 515	Pro AAG Lys	Glu CCA Pro	Gln ATT Ile	ASN ATA Ile	GAA Glu 505 TTT Phe 520	Glu TCC Ser	His ATG Met	Ile GCG Ala	Gly AGG Arg	1574
GAG Glu 495 GTA Val 510	Gln TTA Leu GAC	GAT Asp	GAT Asp	Phe ACC Thr	AAA Lys 5000 TCA Ser 515	Pro AAG Lys	CCA Pro	Gln ATT Ile	ASN ATA Ile	GAA Glu 505 TTT Phe 520	TCC ser	ATG Met	GCG Ala	AGG Arg	
GAG Glu 495 GTA Val 510 CTA Leu	Gln TTA Leu GAC	GAT Asp	GAT Asp	Phe ACC Thr	AAA Lys 500 TCA Ser 515	Pro AAG Lys	CCA Pro	Gln ATT Ile	ASN ATA Ile	GAA Glu 505 TTT Phe 520 GTA Val	Glu TCC Ser	ATG Met	GCG Ala	AGG Arg	1574
GAG Glu 495 GTA Val 510	Gln TTA Leu GAC	GAT Asp	GAT Asp	Phe ACC Thr	AAA Lys 5000 TCA Ser 515	Pro AAG Lys	CCA Pro	Gln ATT Ile	ASN ATA Ile	GAA Glu 505 TTT Phe 520	TCC ser	ATG Met	GCG Ala	AGG Arg	1574

AAG	AAT	GCG	AAA	CTC	AGG	GAA	CTG	GCA	. AAC	CTG	GTT	' GTA	GTG	GCT	1664
Lys	Asn	Ala	Lys	Leu	Arg	Glu	Leu	Ala	Asn	Leu	Val	Val	Val	Ala	
540					545					550					
GGG	TAC	AAT	GAT	GTA	AAA	AAG	TCG	AAT	GAC	AGG	GAG	GAA	ATT	GCC	1709
											Glu				2.00
555	-		•		560	•			•	565					
GAA	ATC	GAG	AAG	ATG	CAC	AGG	CTT	АТА	CAG	GAG	TAT	AAT	TTA	AGA	1754
											Tyr				2.0.
570			-4		575	_				580	-1-				
GGA	CAA	ттт	CGC	TGG	АТТ	GCT	тст	CAA	ACA	ААТ	AGA	СТА	CGA	ልልጥ	1799
											Arg				1755
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										JJJ					
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											Gly				1044
600	014	ДСи	-1-	_	605	110	C _f S	пор	шуз	610	Gly	116	FIIE	ATG	
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CAG	CCT	GC)	ጥጥጥ	ጥልጥ	CAA	GCA	ሙጥጥ	ccc	CTTT	A C A	GTT	CMM	C 2 2	ccc	1889
											Val				1009
	PIO	Ala	File		620	ATG	File	GIY			vaı	Val	GIU	Ala	
615					020					625					
3 m.c	200	mcm	CCT	CIDAD	ccc	ארא	സസ	CCT	N C C	THC C	CAC	CCT	CCTT	003	1024
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	THE	cys	сту			THE	rne	WIG			His	٩ï٨	G.I.V	トだい	
630					635					640					

						TTT Phe 655			1979
						GAA Glu 670		AAG Lys	2024
						ATC Ile 685			2069
						CAA Gin 700			2114
					Gly	TTC Phe 715		GTC Val	2159
			Glu		Arg	TAT Tyr 730			2204
					Asn	TCT Ser 745			2249

ACA	GAT	GAA	GAG	CCT	TCT	ACT	ACT	GAT	GCA	GTT	GCG	ACA	TTC	CGT	2294	
Thr	Asp	Glu	Glu	Pro	Ser	Thr	Thr	Asp	Ala	Val	Ala	Thr	Phe	Arg		
750				,	755					760						
GGA	CCT	TGA	ACGC	TGCT	GC 7	TACI	rgago	T TO	CCAAC	STTGT	GT?	ATATA	ATTA.		2343	
Зlу	Pro	End														
CTGI	'GAAA	AGG A	AATAA	GTGT.	A G	CTACA	CAAA	AGG	TTCT	CAA	CTAT	TAGT	TAT		2393	
CTTC	TCTC	TG T	TAAAT	'AACG	A G	AGTGA	LAAAA	Y TG1	TAATA	ATTG	TTG	ATGTO	CTT		2443	
GAAA	ACTO	AG :	rttgc	TTTG	T TI	'A'I"I'1	"I"I"AA	GTG	TATG	BACA	ATAI	'GT'A'I	l'CA		2493	
,, m,			7 CMMC	יז כיחכ	a mo	יא מוז אי	~ A A A	330	-m x _m	2020	CAMC	~~ ~ ~ ~ ~	-mm		2543	
rat'a	ACGG	AT L	rcttc	AGTG.	A TC	.ATAI	CAAA	AAC	.IACI	GAC	CATC	-GAAG	211		2543	
ል ውጥር	מממנ	ነጥር (	GACAG	CAAC	Δ										2563	
$\mathbf{r}$															2203	

- These sequences can also be combined together in a suitable plasmid which leads to a combination of the individual characteristics, conditioned by the expression of the protein.
- 10 The promoter should ensure that the foreign gene is expressed in the plant. The promoter can be so chosen that the expression occurs only in specified tissues, at a determined time point in the plant's development or at a time point determined by outside influences. The promoter can be homologous or heterologous to the plant. Suitable promoters are e.g. the promoter of the 35S RNA of the cauliflower mosaic virus, the patatin promoter B33 (Rocha-Sosa et al. (1989) EMBO J 8: 23-29) or a promoter

that ensures an expression only in photosynthetically active tissues. Other promoters can be used which ensure an expression only in specified organs, such as the root, tuber, seed, stem or specified cell types such as mesophyllic, epidermal or transport cells.

The coding sequences described herein contain the information for the formation of an mRNA for the large subunit of the ADP-glucose-pyrophosphorylase and the sucrose-phosphate-synthase (SPS) and a part of the 10 information for formation of the small subunit of the ADP-glucose-pyrophosphorylase as well as the sucrose-synthase, that are suitable for the formation of anti-sense RNA to the corresponding genes. Whether a translatable mRNA or an anti-sense nucleic acid is formed, 15 depends on the orientation of the coding sequence in relation to the promoter. If the 3' end of the coding sequence is fused to the 3' end of the promoter, an anti-sense RNA results, and by fusion of the 5' end of the coding to the 3' end of the promoter a translatable RNA 20 results. This latter leads to an increase of the enzyme activity in the cell, whilst the first leads to a reduction of the enzyme activity in the cell.

The coding sequence for the large and small subunit of the ADP-glucose-pyrophosphorylase, the sucrose phosphate synthase and the sucrose synthase can be one of those described in this invention or can be one that is derived by modifications of the sequences described above.

Thereby especially modifications of the sequences can be considered which lead to by-passing of the plant's own regulation mechanisms. Modifications to the DNA sequences of the invention can be by known methods, such as e.g. base exchange or targeted or non-targeted mutagenesis. The so-formed derivatives of the DNA sequences of the invention are also within the scope of the invention.

With plasmids, which contain one or more of the DNA sequences of the invention, sugar beet can be transformed with the object of raising and/or reducing the enzyme activity and/or the change of the sucrose concentration.

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For the introduction of the DNA sequences of the invention in sugar beet, a large number of cloning vectors are available, which contain a replication signal for *E. coli* and a marker, which allows a selection of the transformed cells.

According to the introduction method of the desired gene in the plant, other DNA sequences may be suitable. Should the Ti- or Ri-plasmid be used, e.g. for the transformation of the plant cell, then at least the right boundary, often 15 however both the right and left boundary of the Ti- and Ri-Plasmic T-DNA, is attached, as a flanking region, to the gene being introduced. The use of T-DNA for the transformation of plants cells has been intensively researched and is well described in EP 120 516; Hoekama, 20 In: The Binary Plant Vector System, Offset-drukkerij Kanters B.V. Alblasserdam, (1985), Chapter V; Fraley, et al., Crit. Rev. Plant Sci., 4:1-46 and An et al. (1985) EMBO J. 4: 277-287. Once the introduced DNA is integrated in the genome, it is as a rule stable there and remains 25 also in the offspring of the original transformed cells. It normally contains a selection marker, which induces resistance in the transformed plant cells against a biocide or antibiotic such as kanamycin, G 418, bleomycin, hygromycin or phosphinotricin etc. The individual marker 30 employed should therefore allow the selection of transformed cells from cells, which lack the introduced DNA.

For the introduction of DNA into a plant, besides transformation using Agrobacteria, there are many other

techniques available. These techniques include the fusion of protoplasts, microinjection of DNA and electroporation, as well as ballistic methods and virus infection. From the transformed plant material, whole plants can be regenerated in a suitable medium, which contains antibiotics or biocides for the selection. The resulting plants can then be tested for the presence of introduced DNA. No special demands are placed on the plasmids in injection and electroporation. Simple plasmids, such as e.g. pUC-derivatives can be used. Should however whole 10 plants be regenerated from such transformed cells the presence of a selectable marker gene is necessary. The transformed cells grow within the plants in the usual manner (see also McCormick et al. (1986) Plant Cell Reports 5: 81-84). These plants can be grown normally and crossed 15 with plants, that possess the same transformed genes or different. The resulting hybrid individuals have the corresponding phenotypical properties.

In order to understand the examples forming the basis of this invention all the processes necessary for these tests and which are known per se will first of all be listed:

# 25 1. Cloning process

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The vectors pUC 18/19 and M13mp10 series (Yanisch-Perron et al. (1985) Gene 33: 103-119), as well as the vector EMBL 3 (Frischauf et al. (1983) J Mol Biol 170: 827-842) were used for cloning.

For the plant transformations, the gene constructs were cloned in the binary vector BIN 19 (Bevan (1984) Nucl. Acids Res 12: 8711-8720)

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2. Bacterial strains

The  $E.\ coli$  strain BMH71-18 (Messing et al., Proc. Natl. Acad. Sci. USA (1977), 24, 6342-6346) or TB1 was used for the pUC and M13 mP vectors.

- For the vector BIN19, the *E. coli* strain TB1 exclusively, was used. TB1 is a recombinant-negative, tetracycline-resistant derivative of strain JM101 (Yanisch-Perron et al., Gene (1985), 33, 103-119). The genotype of the TB1 strain is (Bart Barrel, personal communication):
- 10 F'(traD36, proAB, lacI, lacZΔM15), Δ(lac, pro), SupE,
  thiS, recA, Sr1::Tn10(TcR).

The transformation of the plasmids into the potato plants was carried out using Agrobacterium tumefaciens strain

15 LBA4404 (Bevan, (1984), Nucl. Acids Res. 12, 8711-8720).

# 3. Transformation of Agrobacterium tumefaciens

In the case of BIN19 derivatives, the insertion of the DNA into the Agrobacterium was effected by direct transformation in accordance with the method of Holsters et al., (1978) (Mol Gene Genet 163: 181-187). The plasmid DNA of the transformed Agrobacterium was isolated in accordance with the method of Birnboim and Doly (1979)

(Nucl Acids Res 7: 1513-1523) and was analysed by gel electrophoresis after suitable restriction cleavage.

#### 4. Sucrose phosphate-synthase activity test

- The sucrose phosphate-synthase activity was determined according to the method of Siegel and Stitt (1990, Plant Science 66: 205-210) in a two stage analysis. To 180  $\mu$ l of a solution of 50mM HEPES/KOH (pH 7.4), 5mM magnesium chloride, 5mM fructose-6-phosphate, 25mM
- glucose-6-phosphate and 6mM uridine-5'-diphosphoglucose, 20  $\mu l$  of probe was added and incubated for 10 minutes at

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25°C. It was heated for 3 minutes at 95°C, to complete the reaction. After centrifuging, the supernatant was spectroscopically analysed for the liberation of uridine-5'-diphosphate, whereby a pyruvate-kinase coupling enzyme reaction was used. Preparations without hexose phosphate, as well as the measurement of the recovery of added uridine-5'-diphosphate act as controls.

#### Examples

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#### Example 1

Cloning of cDNA to large and small subunits of the ADP glucose pyrophosphorylase of sugar beet.

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From the storage roots of 3-4 month old sugar beet plants grown in the greenhouse, RNA was isolated according to the method of Logemann et al (1987, Anal Biochem 163, 16-20). Resulting from poly-A+-RNA, a cDNA library was laid down according to the method of Gubler and Hoffmann (1983, Gene 25, 263) in the expression vector Lambda Zap II XR. To this there was used an oligo-dT primer provided with an XhoI recognising position and for synthesis of the first cDNA strand methylated cytidine nucleotide was inserted. After synthesis of the two strands an EcoRI-adaptor was attached and removed to one side by again cutting with the restriction endonuclease XhoI. In this way the hemimethylation of cDNA was hindered so that an internal XhoI recognition position is cut. By these procedures there is obtained a population of cDNA molecules, that can be cloned directed into the EcoRI/XhoI cut DNA of the phage Lambda. After packing of recombinant phage-DNA in phage heads, 200000 plaque forming units of the bank were plated out for infection of a bacterial colony and then each is probed with the total cDNA fragment of the large and/or subunit of the AGPase of potato (Müller-Roeber et

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al., 1990, MGG 224, 136-146) as an EcoRI-fragment. The recombinant phages corresponding to the hybridising signal were isolated. By in vivo excision plasmids were cut out from the Lambda zap-genome, which carry a double stranded cDNA as insertion. The plasmids were transformed in bacterial cells. The plasmid-DNA was then propagated in the bacteria. After checking the size of the insertions individual clones were analysed by determination of the primary sequence.

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#### Example 2

Cloning of cDNA to sucrose-phosphate-synthase (SPS) from sugar beet.

From the storage roots of 3-4 month old sugar beet plants grown in the greenhouse, RNA was isolated according to the method of Logemann et al (1987, Anal Biochem 163, 16-20). Resulting from poly-A+-RNA, a cDNA library was laid down 20 according to the method of Gubler and Hoffmann (1983, Gene 25, 263) in the expression vector Lambda Zap II XR. To this there was used an oligo-dT primer provided with an XhoI recognising position and for synthesis of the first cDNA strand methylated cytidine nucleotide was inserted. 25 After synthesis of the two strands an EcoRI-adaptor was attached and removed to one side by again cutting with the restriction endonuclease XhoI. In this way the hemimethylation of cDNA was hindered so that an internal XhoI recognition position is cut. By these procedures 30 there is obtained a population of cDNA molecules, that can be cloned directed into the EcoRI/XhoI cut DNA of the phage Lambda. After packing of recombinant phage-DNA in phage heads, 200000 plaque forming units of the bank were plated out for infection of a bacterial colony and then 35 each is probed with the total cDNA fragment of the

40

sucrose-phosphate-synthase (SPS) from spinach (Sonnewald, 1992, Planta) as NotI. The recombinant phages corresponding to the hybridising signal were isolated. By in vivo excision plasmids were cut out from the Lambda zap-genome, which carry a double stranded cDNA as insertion. The plasmids were transformed in bacterial cells. The plasmid-DNA was then propagated in the bacteria. After checking the size of the insertions individual clones were analysed by determination of the primary sequence.

### Example 3

Cloning of cDNA to sucrose-synthase from sugar beet.

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From the storage roots of 3-4 month old sugar beet plants grown in the greenhouse, RNA was isolated according to the method of Logemann et al (1987, Anal Biochem 163, 16-20). Resulting from poly-A+-RNA, a cDNA library was laid down according to the method of Gubler and Hoffmann (1983, Gene 20 25, 263) in the expression vector Lambda Zap II XR. To this there was used an oligo-dT primer provided with an XhoI recognising position and for synthesis of the first cDNA strand methylated cytidine nucleotide was inserted. After synthesis of the two strands an EcoRI-adaptor was 25 attached and removed to one side by again cutting with the restriction endonuclease XhoI. In this way the hemimethylation of cDNA was hindered so that an internal XhoI recognition position is cut. By these procedures there is obtained a population of cDNA molecules, that can 30 be cloned directed into the EcoRI/XhoI cut DNA of the phage Lambda. After packing of recombinant phage-DNA in phage heads, 200000 plaque forming units of the bank were plated out for infection of a bacterial colony and then parallel is probed with both EcoRI/BgIII sub fragments 35 sucrose synthase from maize (Worrell et al., 1991, Plant

Cell 3, 1121-1130). The recombinant phages corresponding to the hybridising signal were isolated. By in vivo excision plasmids were cut out from the Lambda zap-genome, which carry a double stranded cDNA as insertion. The plasmids were transformed in bacterial cells. The plasmid-DNA was then propagated in the bacteria. After checking the size of the insertions individual clones were analysed by determination of the primary sequence.

#### 10 Example 4

Determination of the nucleotide sequence of the ADP glucose pyrophosphorylase, the sucrose synthase and the sucrose phosphate synthase of sugar beet and derivation of

the corresponding amino acid sequences

The nucleotide sequences of the insertions obtained from Examples 1 -3, were determined by standard methods by means of the dideoxy method (Sanger et al. (1977) Proc.

Natl. Acad. Sci. USA, 74, 5463-5467). The nucleotide sequences and the amino acid sequences derived therefrom are given in the sequence protocols Seq. ID No. 1-4.

The sequences are shown earlier; the protocols are as follows:

42

#### SEQ ID NO: 1

SEQUENCE TYPE: Nucleotide with corresponding protein.

SEQUENCE LENGTH: 1924 base pairs

5 STRANDEDNESS: single

TOPOLOGY: linear
MOLECULE TYPE: cDNA

ORIGINAL SOURCE

10 ORGANISM: Beta vulgaris

IMMEDIATE EXPERIMENTAL SOURCE: cDNA library in Phage Lamda

zap

#### FEATURES:

15 from 206 to 1770 coding region

PROPERTIES: ADP-glucose-pyrophosphorylase, large subunit

### 20 <u>SEQ ID NO: 2</u>

SEQUENCE TYPE: Nucleotide with corresponding protein

SEQUENCE LENGTH: 1763 base pairs

STRANDEDNESS: single

25 TOPOLOGY: linear

MOLECULE TYPE: cDNA

ORIGINAL SOURCE

ORGANISM: Beta vulgaris

30 IMMEDIATE EXPERIMENTAL SOURCE: cDNA library in Phage Lamda

zap

#### FEATURES:

from 3 to 1469 coding region

35

PROPERTIES: ADP-glucose-pyrophosphorylase, small subunit

43

SEQ ID NO: 3

SEQUENCE TYPE: Nucleotide with corresponding protein

SEQUENCE LENGTH: 3635 base pairs

5 STRANDEDNESS: single

TOPOLOGY: linear MOLECULE TYPE: cDNA

ORIGINAL SOURCE

10 ORGANISM: Beta vulgaris

IMMEDIATE EXPERIMENTAL SOURCE: cDNA library in Phage Lamda

zap

FEATURES:

15 from 31 to 3164 coding region

PROPERTIES: Sucrose-phosphate-synthase

20 <u>SEO ID NO: 4</u>

SEQUENCE TYPE: Nucleotide with corresponding protein

SEQUENCE LENGTH: 2563 base pairs

STRANDEDNESS: single

25 TOPOLOGY: linear

MOLECULE TYPE: cDNA

ORIGINAL SOURCE

ORGANISM: Beta vulgaris

30 IMMEDIATE EXPERIMENTAL SOURCE: cDNA library in Phage Lamda

zap

FEATURES:

from 3 to 2300 coding region

35

PROPERTIES: Sucrose synthase

## <u>CLAIMS</u>

DNA sequence with the coding region for die large subunit of ADP-glucose-pyrophosphorylase for the preparation of sugar beet with changed sucrose concentration, characterised in that the sequence has the following nucleotide sequence (Seq. ID No.1):

CAAA	.AGA?	LAA A	CTTC	CCAT	TT TO	CTACT	TCT	TGC	CACA	TAT	AATI	TCCC	CAC		0050
CAAT	TTTT	CT I	TAA <i>T</i> T	ATTTC	CT CA	CTTI	CATI	TAP	ATCAC	TTT	TCAC	CAAC	CAT		0100
TCT	SATAC	CTC C	GACAF	ACCCA	AC TI	TCT	STTCI	r cco	CAAGA	TTC	CAA	ACCTO	CTG		0150
ATTO	TCAT	TC C	CACTA	CATA	rr rı	TGCI	TAT	r TTI	TTTT	CTGG	TTTA	) AAA7	AA		0200
AAGC			AT GO							n Va					0243
			GTT Val											AGT Ser	0288
			AAG Lys											ACT Thr	0333
			GGT Gly											TCT Ser	0378
			TCA Ser											AAA Lys	0423

TAT	GAG	CCA	GCA	TTA	TTT	GAA	TCT	CCA	AAA	GCT	GAC	CCA	AAA	AAT	0468
Tyr	Glu	Pro	Ala	Leu	Phe	Glu	Ser	Pro	Lys	Ala	Asp	Pro	Lys	Asn	
	75					80					85				
											ACT				0513
Val		Ala	Ile	Val	Leu		Gly	Gly	Ala	Gly	Thr	Arg	Leu	Phe	
	90					95					100				
						<b>7.0</b> T		223	663	cmc	003	» mm	CCA	ccc	0550
											CCA				0558
Pro		Thr	Ser	Arg	Arg		гÀг	Pro	Ala	vaı	Pro	TIE	GIÀ	GIY	
	105					110					115				
mcm	ma c	NCC.	CTC	አጥጥ	GAT	GTG.	CCT	ልጥር	<b>A</b> GC	220	TGC	ልጥር	AAC	AGT	0603
											Cys				
Cys	120	ALG	пси	110	p	125					130		-		
	120														
GGC	ATT	AGA	AAG	ATT	TTC	ATT	CTT	ACC	CAG	TTC	AAT	TCG	TTT	TCG	0648
Gly	Ile	Arg	Lys	Ile	Phe	Ile	Leu	Thr	Gln	Phe	Asn	Ser	Phe	Ser	
	135					140					145				
											GGA				0693
Leu	Asn	Arg	His	Leu	Ala	Arg	Thr	Tyr	Asn	Phe	Gly	Asp	Gly	Val	
	150					155					160				
						<b>6</b> 50	a.a	amm.	mmm	COM	com	202	C	7.07	0720
														ACA	0738
Asn		GIŸ	Asp	GIĀ	rne		GIU	val	Fue	WIG	Ala 175	TIIL	GIII	TIIT	
	165					170					1/3				

			TCA												0783
Pro	Gly	Glu	Ser	Gly	Lys	Lys	Trp	Phe	Gln	Gly	Thr	Ala	Asp	Ala	
	180					185					190				
GTA	AGA	CAG	TTT	TTC	TGG	GCA	TTT	GAG	GAT	TCC	AAA	TCC	AAG	GAT	0828
Val	Arq	Gln	Phe	Phe	Trp	Ala	Phe	Glu	Asp	Ser	Lys	Ser	Lys	Asp	
	195					200					205				
стс	GAG	CAT	АТА	GTT	ATT	TTA	TCC	GGT	GAT	CAT	CTT	TAC	CGA	ATG	0873
		His													
	210					215		_	_		220				
таэ	TAC	ATG	AGT	TTT	TGG	CAG	AAG	CAC	ATT	GAC	ACC	AAT	GCT	GAT	0918
		Met													
F	225				-	230	_			_	235				
АТТ	ACA	GTG	TCA	TGC	ATA	ccc	ATG	GAT	GAC	AGC	CGT	GCA	TCG	GAT	0963
		Val													
	240			•		245		_	_		250				
	2.0														
ጥልጥ	GGG	CTG	ATG	AAG	ATT	GAT	CAC	ACT	GGA	CGC	ATT	GTC	CAT	TTT	1008
		Leu													
- 1 -	255			-,		260			-	•	265				
	233														
CCA	GAA	AAA	CCC	AAG	GGT	TCT	GAT	CTA	ACA	GCA	ATG	CAA	GTA	GAT	1053
		Lys													
Ald		ny s	FIO	درر	-17	275					280			•	
	270					2.5									

ACA	ACT	GTT	C.L.I.	GGG	CTC	TCT	GAC	CTT	GAA	GCT	ATG	TCA	AAT	CCA	1098
Thr	Thr	Val	Leu	Gly	Leu	Ser	Asp	Leu	Glu	Ala	Met	Ser	Asn	Pro	
	285					290					295				
m a m	N TO TO	CCA	<b>ጥ</b> ር እ	እሞር	CCT	CTT	ጥልጥ	ĠͲC	ተተ	CGA	ACG	CAT	стт	Cdrdr	1143
															1143
Tyr		Ата	ser	Mec	GIY		ıyı	AGI	riie	Arg	Thr	ASP	Val	Deu	
	300					305					310				
ATG	GAG	CTT	CTC	AAT	CGA	AAA	TAC	CCT	TCA	AGC	AAT	GAT	TTT	GGC	1188
Met	Glu	Leu	Leu	Asn	Arg	Lys	Tyr	Pro	Ser	Ser	Asn	Asp	Phe	Gly	
	315					320					325				
TCT	GAG	ATT	ATT	CCT	TCA	GCT	GTA	GGA	GAG	TCT	AAT	GTT	CAG	GCA	1233
											Asn				
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															1276
Tyr		Pne	Asn	Asp	Tyr		GIU	Asp	116	GIÀ	Thr	116	гуу	ser	
	345					350					355				
											CCT				1323
Phe	Phe	Asp	Ser	Asn	Leu	Ala	Leu	Thr	Gln	Gln	Pro	Pro	Lys	Phe	
	360					365					370				
GAA	TTC	TAC	GAT	CCA	AAA	ACA	CCT	TTT	TAT	ACA	TCT	GCA	AGA	TTT	1368
											Ser				
	375	-1-			- 4 -	380			-		385		-		
	212					300									

CTG	CCT	CCT	ACA	AAA	GTC	GAC	AGG	TGC	AAG	ATT	GTC	GAT	TCC	ATT	1413
Leu	Pro	Pro	Thr	Lys	Val	Asp	Arg	Cys	Lys	Ile	Val	Asp	Ser	Iļe	
	390					395					400				
CTA	ጥርር	САТ	GGT	TGT	TTT	CTA	CAG	GAG	TCT	AGC	ATC	CAA	CAT	TCC	1458
			Gly												
VQI	405		Q I J	0,70		410					415				
	403														
	c.mm	ccm	GTT	ccc	ጥሮል	AC A	מיזיים	GAG	тсс	GGG	GTT	GAG	TTC	CAG	1503
			Val												
Ile		GIY	vaı	Arg	261	425	Leu	GIU	Jer	O L J	430				
	420					425					430				
						663	C N CI	ma c	mam	C	л СТ	CDD	ጥርኔ	GAA	1548
			ATG												20.0
Asp		Met	Met	Met	GIY		ASP	Tyr	TYL	GIII		Giu	Ser	014	
	435					440					445				
											c.mm	C C M	CTC	C.C. y	1593
			CTG												1090
Ile	Ala	Ser	Leu	Leu	Ala	•	Gly	Lys	Val	Pro		GIY	vai	GTĀ	
	450					455					460				
			AAA												1638
Gln	Asn	Thr	Lys	Ile	Lys	Asn	Cys	Ile	Ile	Asp	Lys	Asn	Ala	Lys	
	465					470					475				
									•						
ATT	GGA	AAA	GAT	GTG	GTA	ATC	GCA	AAC	ACG	GAT	GGT	GTT	GAG	GAA	1683
			Asp												
	480		-			485					490				

GCA	GAT	AGA	CCA	AAT	GAA	GGC	TTT	TAC	ATC	AGG	TCG	GGC	ATT	ACC	1728
Ala	Asp	Arg	Pro	Asn	Glu	Gly	Phe	Tyr	Ile	Arg	Ser	Gly	Ile	Thr	
	495					500					505				
ATC	ATT	TTG	AAG	AAC	GCA	ACC	ATA	CAA	GAC	GGT	CTT	GTG	ATT	TAG	1773
Ile	Ile	Leu	Lys	Asn	Ala	Thr	Ile	Gln	Asp	Gly	Leu	Val	Ile	End	
	510					515					520				
ATT!	гаатс	CAT A	AACCI	CATI	A GA	LAAG!	AATA	ATT	TTG	CATG	ATT	rccti	TTT		1823
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A															1924
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			Val												
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СТС	GCA	ттс	TCC	тст	TCT	тст	CTC	TCC	GGC	GAC	AAA	ATT	CAA	ACG	0089
			Ser												
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			Leu												
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30					دد					40					

CCG	ATT	GTT	GTC	TCT	ccc	AAA	GCT	GTT	TCT	GAT	TCT	AAG	AAT	TCG	0179
Pro	Ile	Val	Val	Ser		Lys	Ala	Val	Ser		Ser	Lys	Asn	Ser	
45					50					55					
CAG	ACT	TGT	CTT	GAC	CCT	GAA	GCC	AGC	CGT	AGT	GTT	CTT	GGT	ATT	0224
Gln	Thr	Cys	Leu	Asp	Pro	Glu	Ala	Ser	Arg	Ser	Val	Leu	Gly	Ile	
60					65					70					
										<b></b>	200	mmc	3 CM	226	0260
			GGT												0269
	Leu	GIY	Gly	GIY		GIY	THE	Arg	reu	85	PIO	rea	TIIL	пуз	
75					80					65					
AAG	AGA	GCC	AAA	CCA	GCC	GTG	CCA	CTC	GGT	GCT	AAT	TAT	AGG	CTT	0314
Lys	Arg	Ala	Lys	Pro	Ala	Val	Pro	Leu	Gly	Ala	Asn	Tyr	Arg	Leu	
90					95					100					
<b>&gt;</b>	C A M	3 M.C	CCA	CTC	NGC.	ስ ልጥ	ייכיי	ጥጥር	<b>11</b>	ΔСΤ	አልጥ	Δጥጥ	TCC	AAA	0359
			Pro												
105	nap	110	110		110		-1-			110				•	
200												•			
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			CTT												0404
Ile	Tyr	Val	Leu	Thr	Gln	Phe	Asn	Ser	Ala		Leu	Asn	Arg	His	
115					120					125					
CTT	TCG	CGG	GCA	TAT	GCT	AGC	AAC	ATG	GGA	GGA	TAC	AAA	AAT	GAG	0449
Leu	Ser	Arg	Ala	Tyr	Ala	Ser	Asn	Met	Gly	Gly	Tyr	Lys	Asn	Glu	
130					135					140					
						•									
ccc	ന്നസ	כתיא	GAA	ርጥጥ	Curu	GCT	GCT	CAG	CAA	AGፓ	CCA	GAG	<b>አ</b> ልጥ	CCA	0494
			Glu												
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145															

					AGG Arg 170				0539
				Tyr	TTG Leu 185		•		0584
				Arg	TTT Phe 200				0629
					GCA Ala 215				0674
				Met	AAA Lys 230			GAA Glu	0719
					AAA Lys 245			TTG Leu	0764
					GGT Gly 260				0809

AGA	GCA	AAA	GAA	ATG	CCA	TTC	ATA	GCC	AGC	ATG	GGC	ATA	TAT	GTT	0854
Arg	Ala	Lys	Glu	Met	Pro	Phe	Ile	Ala	Ser	Met	Gly	Ile	Tyr	Val	
265					270					275					
ATT	AGC	AAA	GAT	GTA	ATG	CTT	AAT	CTG	CTT	CGG	GAG	CAA	TTT	CCT	0899
Ile	Ser	Lys	Asp	Val	Met	Leu	Asn	Leu	Leu	Arg	Glu	Gln	Phe	Pro	
280		_			285					290					
GGT	GCT	AAT	GAT	TTT	GGA	AGT	GAA	GTT	ATT	CCA	GGC	GCC	ACT	TCC	0944
Glv	Ala	Asn	Asp	Phe	Gly	Ser	Glu	Val	Ile	Pro	Gly	Ala	Thr	Ser	
295			_		300					305					
ATA	GGG	TTG	AGA	GTC	CAA	GCT	TAT	TTG	TAT	GAT	GGT	TAC	TGG	GAG	0989
Ile	Gly	Leu	Arg	Val	Gln	Ala	Tyr	Leu	Tyr	Asp	Gly	Tyr	Trp	Glu	
310					315					320					
GAT	ATT	GGT	ACC	ATT	GAA	GCT	TTT	TAC	AAT	GCT	AAC	TTG	GGA	ATC	1.054
Asp	Ile	Gly	Thr	Ile	Glu	Ala	Phe	Tyr	Asn	Ala	Asn	Leu	Gly	Ile	
325					330					335					
ACC	AAA	AAG	CCG	GTG	CCA	GAT	TTT	AGC	TTC	TAT	GAT	CGT	TCA	TCT	1079
Thr	Lys	Lys	Pro	Val	Pro	Asp	Phe	Ser	Phe	Tyr	Asp	Arg	Ser	Ser	
340					345					350					
CCA	ATT	TAT	ACA	CAA	CCT	CGG	TAT	TTG	CCT	CCT	TCA	AAG	ATG	CTT	1124
Pro	Ile	Tyr	Thr	Gln	Pro	Arg	Tyr	Leu	Pro	Pro	Ser	Lys	Met	Leu	
355					360	•				365					

			ATA Ile	Thr					Gly						1169
			AAG Lys						Ile						1214
			GGT Gly												1259
GAT Asp			GAG Glu												1304
			CCT Pro		GGA Gly					CGT Arg					1349
GTC Val	AAG Lys	ATT Ile	ATC	AAC Asn	AGT Ser	GAC Asp	AAT Asn	GTA Val	CAA Gln	GAA Glu	GCA Ala	GCA Ala	AGA Arg	GAA Glu	1394
445 ACA Thr	GAC	GGA Gly	TAC Tyr	TTC Phe	ATA	AAG Lys	AGC Ser	GGA Gly	ATA Ile	Val	ACT Thr	ATA Ile	ATC	AAG Lys	1439
460					465					470					

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								•	-						
			ATT								AAAT	GGAG	CA		1482
Asp	Ala	Met	Ile	Pro	Ser	Gly	Thr	Val	Ile	End					
475					480					485					
															1633
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TGA	CCTT	TG A	ATTC	AATCI	lur un	LAGI.	IAIG.	I AAF	,121		3001				
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TGG	SCAC!	CAA .	AAAT!	rtgg:	CA AT	rgct	ATAC	C AAA	LATA	ATA	AAAA	GATC	TT		1732
GCT	GGT	rtt (	GGTA	AAAA	AA AA	AAAA	AAAA	A A							1763
	3.		DNA s	_											
		-	phosp										or s	ugar	
			beet										o fo	Jlow	ina
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5		1	nucle	eotic	ie se	equei	ice	(seq.	. 10	NO.	,,.				
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			Ser												
-				10					15					20	
						•									
			GCA												0134
Leu	Asp	Asp	Ala	Lys	Ser	Ser	Leu	Leu	Leu	Arg	Glu	Arg	Gly		
				25					3.0					35	

$\mathtt{TTT}$	AGT	CCT	ACT	CGT	TAC	TTT	GTT	GAA	GAA	GTT	ATC	ACT	GGT.	TTT	01/9
Phe	Ser	Pro	Thr	Arg	Tyr	Phe	Val	Glu	Glu	Val	Ile	Thr	Gly	Phe	
				40					45					50	
GAT	GAA	ACC	GAC	CTT	CAT	CGT	TCA	TGG	GTT	CGG	GCA	CAA	GCA	ACA	0224
			Asp												
			_	55					60					65	
AGG	AGT	CCT	CAA	GAG	AGG	AAT	ACT	AGA	TTG	GAG	AAC	ATG	TGT	TGG	0269
			Gln												
9		•		70					75					80	
AGA	A ጥጥ	TGG	AAT	TTG	GCT	CGT	CAG	AAG	AAG	CAG	CTT	GAG	AAT	GAA	0314
			Asn												
9				85		•		•	90					95	
GAA	GCT	CAG	CGG	AAG	ACA	AAA	CGT	CGT	ATG	GAG	CTT	GAG	AGG	GGT	0359
			Arg												
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ССТ	CGA	GAA	GCA	ACT	GCT	GAT	ATG	TCG	GAG	GAC	TTA	TCA	GAA	GGC	0404
			Ala												
9				115		-			120					125	
GAA	AAG	GAC	ATT	TCA	GCT	CAT	GGT	GAT	AGC	ACC	CGT	CCT	AGA	TTG	0449
			Ile												
010	2,2			130					135					140	
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CCA	AGA	ATA	AAT	TCT	CTT	GAT	GCT	ATG	GAG	ACA	TGG	ATT	AGT	CAA	0494
														Gln	
ELU	ALG			145		•			150					155	

												CTT			0539
Gln	Lys	Glu	Lys	Lys	Leu	Tyr	Leu	Val	Leu	Ile	Ser	Leu	His	Gly	
				160					165					170	
ттG	АТА	CGA	GGT	GAA	AAC	ATG	GAA	CTT	GGC	CGT	GAT	TCT	GAT	ACT	0584
												Ser			
			_	175					180					185	
			-mm		m » m	CTC	CETT	CNC	CTTT	CCA	) CC	GCT	СТА	GGT	0629
												Ala			
GIÀ	GIÀ	GIN	vai	190	TYL	vai	Val	Giu	195	NIG	n. 9			200	
				190					100						
TCG	ATG	CCA	GGT	GTT	TAT	AGA	GTT	GAT	TTG	CTA	ACT	AGG	CAA	GTT	0674
Ser	Met	Pro	Gly	Val	Tyr	Arg	Val	Asp	Leu	Leu	Thr	Arg	Gln	Val	
				205					210					215	
TCA	тст	CCT	GAC	GTG	GAT	TGG	AGT	TAT	GGG	GAG	CCT	ACT	GAG	ATG	0719
												Thr			
			-	220					225					230	
		203	200	CAM	TCC	יחממ	CCT	արար	ሮልጥ	САТ	GAT	GAT	GAT	GAA	0764
												Asp			
Leu	Asn	Pro	Arg	235	Ser	ASII	Gry	1110	240	1.05		1101		245	
				233					• • •						
					0.05	com	m > C	) mm	cmm	CCm	א יחי ל	CCN	ተነጥጥ	GGG	0809
												Pro		GGG	
Met				V 0 7	1-1V	AIA	IVI	$\perp$	val	TT Y	TTE	FLU	* ***	~ ~ y	
	Gly	Giu	261	250	O ₊ ,		-1-		255					260	

CCG	AGG	GAT	AAG	TAT	ATC	GCA	AAA	GAA	GAG	CTT	TGG	CCC	TAT	ATT	0854
Pro	Arg	Asp	Lys	Tyr	Ile	Ala	Lys	Glu	Glu	Leu	Trp	Pro	Tyr	Ile	
				265					270					275	
CCT	GAA	TTT	GTT	GAT	GGT	GCT	CTA	AAC	CAC	ATA	GTT	CAA	ATG	TCC	0899
Pro	Glu	Phe	Val	Asp	Gly	Ala	Leu	Asn	His	Ile	Val	Gln	Met	Ser	
				280					285					290	
AAA	GTT	TTA	GGT	GAG	CAA	ATT	GGT	AGC	GGG	GAA	ACA	GTT	TGG	CCA	0944
Lys	Val	Leu	Gly	Glu	Gln	Ile	Gly	Ser	Gly	Glu	Thr	Val	Trp	Pro	
				295					300					305	
			CAT												0989
Val	Ala	Ile	His	Gly	His	Tyr	Ala	Asp	Ala	Gly	Asp	Ser	Ala	Ala	
				310					315					320	
			GGT												1034
			GGT Gly						Met				Gly	His	1034
													Gly		1034
				Gly					Met				Gly	His	1034
Leu	Leu	Ser	Gly	Gly 325	Leu	Asn	Val	Pro	Met 330	Leu	Leu	Thr	Gly	His 335	
Leu	Leu	Ser GGC	Gly CGA	Gly 325 GAC	Leu	Asn TTA	Val	Pro	Met 330 CTC	Leu	Leu AAA	Thr	Gly	His 335 CGA	1034
Leu	Leu	Ser GGC	Gly	Gly 325 GAC Asp	Leu	Asn TTA	Val	Pro	Met 330 CTC Leu	Leu	Leu AAA	Thr	Gly GGT Gly	His 335 CGA Arg	
Leu	Leu	Ser GGC	Gly CGA	Gly 325 GAC	Leu	Asn TTA	Val	Pro	Met 330 CTC	Leu	Leu AAA	Thr	Gly GGT Gly	His 335 CGA	
Leu	Leu	Ser GGC	Gly CGA	Gly 325 GAC Asp	Leu	Asn TTA	Val	Pro	Met 330 CTC Leu	Leu	Leu AAA	Thr	Gly GGT Gly	His 335 CGA Arg	
Leu TCT Ser	Leu CTT Leu	Ser GGC Gly	Gly CGA Arg	Gly 325 GAC Asp 340	Leu AAG Lys	Asn TTA Leu	Val GAG Glu	Pro CAG Gln	Met 330 CTC Leu 345	Leu CTC Leu	Leu AAA Lys	Thr CAG Gln	Gly GGT Gly	His 335 CGA Arg 350	1079
TCT Ser	Leu CTT Leu TCT	GGC Gly	Gly CGA Arg	Gly 325 GAC Asp 340	Leu AAG Lys	TTA Leu	Val GAG Glu AAT	Pro CAG Gln	Met 330 CTC Leu 345	CTC Leu	AAA Lys ATA	Thr CAG Gln	Gly GGT Gly CGT	His 335 CGA Arg 350	
TCT Ser	Leu CTT Leu TCT	GGC Gly	Gly CGA Arg	GAC Asp 340 GAC	Leu AAG Lys	TTA Leu	Val GAG Glu AAT	Pro CAG Gln	Met 330 CTC Leu 345 TAC	CTC Leu	AAA Lys ATA	Thr CAG Gln	GIY GGT GIY CGT Arg	His 335 CGA Arg 350 AGG Arg	1079
TCT Ser	Leu CTT Leu TCT	GGC Gly	Gly CGA Arg	Gly 325 GAC Asp 340	Leu AAG Lys	TTA Leu	Val GAG Glu AAT	Pro CAG Gln	Met 330 CTC Leu 345	CTC Leu	AAA Lys ATA	Thr CAG Gln	GIY GGT GIY CGT Arg	His 335 CGA Arg 350	1079

ATA	GAA	GCC	GAA	GAG	TTA	TCA	CTT	GAT	GCC	TCT	GAG	ATA	GTC	ATA	1169
Ile	Glu	Ala	Glu	Glu	Leu	Ser	Leu	Asp	Ala	Ser	Glu	Ile	Val	Ile	
				370					375					380	
ACT	AGT	ACA	AGA	CAA	GAA	ATA	GAA	GAG	CAA	TGG	CAC	CTC	TAT	GAT	1214
		Thr													
			_	385					390					395	
GGG	ттт	GAT	CCT	GTG	CTA	GAA	CGT	AAA	CTC	CGT	GCT	AGG	ATG	AAG	1259
		Asp													
Cly				400			-	-	405					410	
CGT	GGT	GTA	AGC	TGT	TAT	GGA	AGG	TTC	ATG	ccc	CGG	ATG	GTT	GTT	1304
		Val													
9	1			415	•	-	_		420					425	
ጥጥል	ССТ	CCT	GGA	ATG	GAA	TTC	AAT	CAT	ATT	GTT	CCA	CAT	GAG	GGT	1349
		Pro													
			2	430					435					440	
									,	•					
ርልጥ	ልጥር	GAT	GGT	GAA	ACA	GAA	GAA	ACT	GAA	GAG	CAT	CCT	ACA	TCA	1394
		Asp													
rsp			1	445					450					455	
CCT	ር እጥ	CCA	ССТ	ATC	TGG	GCT	GAG	ATT	ATG	CGC	TTC	TTT	TCT	AAA	1439
		Pro													
PIO	wsh	FIU	110	460					465	,				470	
				-00											

CCA	AGG	AAG	CCA	ATG	ATA	CTT	GCC	CTT	GCT	AGG	CCT	GAC	CCG	AAG	1484
Pro	Arg	Lys	Pro	Met	Ile	Leu	Ala	Leu	Ala	Arg	Pro	Asp	Pro	Lys	
				475					480					485	
														CCA	1529
Lys	Asn	Ile	Thr	Thr	Leu	Val	Lys	Ala	Phe	Gly	Glu	Cys	Arg	Pro	
				490					495					500	
				GCT											1574
ren	Arg	GIU	Leu	Ala	ASI	Leu	THE	rea		met	GIY	ASI	_	_	
				505					510					515	
GGT	ATT	GAC	GAG	ATG	TCA	AGC	ACC	AGT	TCT	TCA	GTT	CTC	CTG	TCA	1619
				Met											
•		-		520					525					530	
GTG	CTT	AAG	CTA	ATT	GAT	CAA	TAC	GAC	CTT	TAT	GGT	CAA	GTA	GCA	1664
Val	Leu	Lys	Leu	Ile	Asp	Gln	Tyr	Asp	Leu	Tyr	Gly	Gln	Val	Ala	
				535					540					545	
				CAC											1709
Tyr	Pro	Lys	His	His	Lys	Gln	Ala			Pro	Glu	Ile			
				550					555		•			600	
						•									
mmc	CCA	CCA	እ ስ C	ACA	<b>33C</b>	GG N	CTC	ሙሙጥ	א ידיתי	יייממ	CCA	CCT	መጥጥ	<b>አ</b> ጥጥ	1754
				Thr											1754
nen	WIG	MIG	ב גיה	605	μys	GIY	• u 1		610	ייכה	z a O	710		11E 615	
				505					710					-15	

GAG	CCA	TTT	GGG	CTG	ACT	CTA	ATA	GAG	GCA	GCA	GCT	CAT	GGT	TTA	1799
Glu	Pro	Phe	Gly	Leu	Thr	Leu	Ile	Glu	Ala	Ala	Ala	His	Gly	Leu	
				620					625					630	
CCG	ATG	GTT	GCT	ACG	AAA	AAT	GGA	GGC	CCT	GTT	GAT	ATC	CAG	AGG	1844
			Ala												
				635					640					645	
GTC	CTT	GAT	AAT	GGT	CTT	CTT	GTG	GAT	CCT	CAT	GAG	CAG	CAG	TCT	1889
			Asn												
		-		650					655					660	
ATT	GCT	ACT	GCT	TTG	CTG	AAG	CTT	GTT	GCT	GAT	AAG	CAA	CTA	TGG	1934
			Ala												
				665					670		٠			675	
				٠											
ACA	AAA	TGC	CAG	CAA	AAT	GGA	CTG	AAA	AAT	ATT	CAT	CTC	TAC	TCT	1979
Thr	Lys	Cys	Gln	Gln	Asn	Gly	Leu	Lys	Asn	Ile	His	Leu	Tyr	Ser	
				680					685					690	
TGG	CCA	GAG	CAT	TCG	AAG	ACA	TAC	CTA	TCT	CGA	ATA	GCC	AGT	TCG	2024
Trp	Pro	Glu	His	Ser	Lys	Thr	Tyr	Leu	Ser	Arg	Ile	Ala	Ser	Ser	
-				695					700					705	
						•									
AGA	CAA	AGG	CAA	CCA	CAG	TGG	CAA	AGA	AGT	AGT	GAT	GAA	GGG	CTT	2069
			Gln												
•		_		710					715					720	

GAC	AAT	CAA	GAG	CCT	GAA	TCT	CCA	AGT	GAT	TCT	TTA	AGA	GAT	ATA	2114
Asp	Asn	Gln	Glu	Pro	Glu	Ser	Pro	Ser	Asp	Ser	Leu	Arg	Asp	Ile	
				725					730					735	
AAG	GAT	ATA	TCT	CTA	AAC	CTT	GAA	GTT	CTC	GTT	AGA	CCG	GAG	AAA	2159
Lys	Asp	Ile	Ser	Leu	Asn	Leu	Glu	Val	Leu	Val	Arg	Pro	Glu	Lys	
				740					745					750	
AGG	GTG	AAG	ACG	TTG	AAA	ATC	TTG	GGA	TTG	ATG	ACA	AAA	GCA	AAT	2204
Arg	Val	Lys	Thr	Leu	Lys	Ile	Leu	Gly	Leu	Met	Thr	Lys	Ala	Asn	
				755					760					765	
									AAT						2249
Ser	Arg	Met	Leu	Leu	Cys	Ser	Trp	Ser	Asn	Gly	Val	His	Lys	Met	
				770					775				•	780	
									GTA						2294
Leu	Arg	Lys	Ala		Phe	Ser	Asp	Lys	Val	Asp'	Gln	Ala			
				785					790				•	795	
	<b>~</b> ~ ~		CC3	<b></b>	n.c.c	3.00	202		C TT TT	אתיא	תו אינו	C TP (T)	א תייחי	CCTT	2339
									CTT						2339
гàг	Tyr	Pro	Ala		Arg	Arg	Arg		Leu	116	TYL	vai		810	
				800					805				•	810	
											-				
ርሞአ	GA C	GGG	CAT	ጥልጥ	GAA	GAT	GGA	CTT	TTT	GAT	АТТ	GTT	CGG	AGG	2384
									Phe						
4 G T	nop	G ± y		815	~~~		1		820	-1-1-				825	
														•	

ATA	TTT	GAT	GCT	GCT	GGC	AAG	GAG	AAG	ATT	GAA	GG.I.	TCC	ATC	GGG	2429
Ile	Phe	Asp	Ala	Ala	Gly	Lys	Glu	Lys	Ile	Glu	Gly	Ser	Ile	Gly	
		_		830					835					840	
mmm.	3 (11 3	mm/C	ጥርል	<b>A</b> C A	ሞርር	ጥልጥ	тст	ATG	CCC	GAA	ATT	CAG	AAC	TAT	2474
													Asn		
Pne	TIE	Den	Ser		361	- 7 -	001		850					855	
				845					830					000	
									<b>61</b> m	<b></b>	G 3 M	CO2	mam	N CO N	2519
													TAT		2313
Leu	Leu	Ser	Lys	Gly	Phe	Asn	Leu	His		Phe	Asp	Ala	Tyr		
				860					865					870	
													TCA		2564
Cys	Asn	Ser	Gly	Ser	Glu	Leu	Tyr	Tyr	Ser	Ser	Leu	Asn	Ser	Glu	
				875					880					885	
GAG	AGT	AAT	ATT	ATA	GCA	GAT	TCA	GAT	TAC	CAT	.TCA	CAC	ATA	GAG	2609
Glu	Ser	Asn	Ile	Ile	Ala	Asp	Ser	Asp	Tyr	His	Ser	His	Ile	Glu	
				890					895					900	
መእር	»C»	TGG	сст	GGA	GAA	GGC	CTT	AGA	AGG	ACT	TTG	CTT	CGC	TGG	2654
													Arg		
TYE	ALG	пр	GIY	905	014		200		910					915	
				905					720						
					~ 3 3		<b>አ</b> አጠ	CCM	CAA	220	כאא	CAA	CAG	Cum	2699
													CAG		2000
Ala	Ala	Ser	Ile		Glu	гÀг	ASN	GIĀ		AST	GIU	GIU	Gln		
				920					925					930	

ATT	ACT	GAA	GAT	GAA	GAA	GTT	TCT	ACG	GGT	TAT	TGC	TTT	GCG	TTT	2744
Ile	Thr	Glu	Asp	Glu	Glu	Val	Ser	Thr	Gly	Tyr	Cys	Phe	Ala	Phe	
				935					940				9	945	
									CCT						2789
Lys	Ile	Lys	Asn	Gln	Asn	Lys	Val	Pro	Pro	Thr	Lys	Glu	Leu	Arg	
				950					955				!	960	
•					•										
									TGC						2834
Lys	Ser	Met	Arg	Ile	Gln	Ala	Leu	Arg	Cys	His	Val	Ile			
				965					970				!	975	
															. 056
									CCA						2879
Gln	Asn	Gly	Ser		Met	Asn	Val	Ile	Pro	Val	Leu	Ala			
				980					985					990	
	<b></b>	660	CTIC.	200	ጥእጥ	CTT	ייימייי	CTT	CGT	TGG	GGA	CTT	GAG	TTG	2924
									Arg						
ser	GIN	WIG	Leu	995	- 7 -	Dea	-1-		1000		1			005	
				223				-							
ጥርር	AAG	ATG	GTT	GTC	TTT	GTT	GGA	GAA	TGT	GGT	GAC	ACA	GAT	TAT	2969
									Cys						
001	_1_			1010			_		1015					020	
						•									
GAA	GGC	TTG	CTT	GGC	GGG	GTC	CAT	AAA	ACC	GTA	ATA	CTG	AAG	GGA	3014
									Thr						
	•			1025					1030					035	

TCC	AAC	ACT	GCT	TTA	AGG	TCT	CTC	CAT	GCC	AAC	AGA	AGT	TAC	3055
Ser	Asn	Thr	Ala	Leu	Arg	Ser	Leu	His	Ala	Asn	Arg	Ser	Tyr	
		1	1040				1	.045				1	050	
									•					
CTT	TCA	CAT	GTC	GTG	TCG	CTT	GAC	AGC	ccc	AAT	ATT	GGC	GAG	3104
Leu	Ser	His	Val	Val	Ser	Leu	Asp	Ser	Pro	Asn	Ile	Gly	Glu	
			1055				1	.060				1	065	
AGC	AAA	GGG	TGC	AGC	AGC	TCC	GAG	ATC	CAG	TCC	ATC	GTC	ACA	3149
	_•													
CTC	TCC	AAA	GCT	TAA	TCAC	SATAS	CT (	CTG	CTTTC	T T:	rTGG	GTAA	G	3197
GTT	CA '	TCTT	ATATO	SA T	ratai	CAT	A AG	ATAC:	ATA	TAAC	CAC	CTT		3247
GTA	AGT	CAGT	CCCA	ra at	raat <i>i</i>	AATG	r AC	TCAC	GAAC	CAC	ATA	CTT		3297
GTT	GT '	TCAG	ragto	GA T	ragro	CTCA	r AA:	TAAT	CATA	TAA	TAC	ACA		3347
	_													
CTG	CTA .	ACTA	GTGG:	ra as	ratc:	raag	C TC	AACA	AATA	AGA:	rgta.	AAA		3391
PAGT	ATG	GAAA:	rgaa'	TT G	CTAG	CTGT:	r GA	rcrc:	TTTC	CCT'	TAT	TCT		344
יידי אַ ידיי	יייכ	тттс	CTCA!	rc T	CATG:	raaa.	A AC	AATT	TTCT	GAA	GTG'	TAC		349
ուսար	יירר	<u>ርርጥ</u> ጥ:	ייערים	ልጥ ሮ	rgrar	TAT'	r TC	ract?	TTT	TTT	STTT	GTA		354
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. ሙ ጽ ጥ <i>ነ</i>	-Cm	ርጥር እ '	ኮርር እሳ	3G A	GTGA	ישאאי	r aa	ATAA	CCGG	CTT	GCTA.	AAT		359
TAT	1	CICH.	LCGM											
	CTT Leu  AGC Ser  CTC Leu  GGTAA  GTTC  TAGTA	SET ASN  CTT TCA  Leu Ser  AGC AAA  Ser Lys  CTC TCC  Leu Ser  GGTTTCA  GGTAAGT  AGTTGGT  GCTGTTA  TAGTATG  TTATTTC	SET ASN Thr  CTT TCA CAT  Leu Ser His  AGC AAA GGG  Ser Lys Gly  CTC TCC AAA  Leu Ser Lys  GGTTTCA TCTT  GGTAAGT CAGT  GGTAGT TCAGT  GCTGTTA ACTAG  TAGTATG GAAA  TTATTTC TTTCC	Ser Asn Thr Ala  1040  CTT TCA CAT GTC  Leu Ser His Val  1055  AGC AAA GGG TGC  Ser Lys Gly Cys  1070  CTC TCC AAA GCT  Leu Ser Lys Ala  1085  GGTTTCA TCTTATATO  GGTAAGT CAGTCCCAT  AGTTGGT TCAGTAGTC  GCTGTTA ACTAGTGGT  TATTTC TTTCCTCAT  CTTTTTCC CCTTATATATO  CTTTTTCC CCTTATATATATATATATATATATATATATA	Ser Asn Thr Ala Leu 1040  CTT TCA CAT GTC GTG Leu Ser His Val Val 1055  AGC AAA GGG TGC AGC Ser Lys Gly Cys Ser 1070  CTC TCC AAA GCT TAA Leu Ser Lys Ala End 1085  GGTATCA TCTTATATGA TGGTA AGG GGTAGT CAGTCCCATA AGG GGTAGT TCAGTAGTGA TGGTTGGT TCAGTAGTGA TGGTTGGT TCAGTAGTGA TGGTTATTC TTTCCTCATC TGGTTTTTCC CCTTATATAT CGGTTTTTCC CCTTATATAT CGGTTTTTCC CCTTATATAT CGGTTTTTCC CCTTATATAT CGGTTTTTTCC CCTTATATAT CGGTTTTTCC CCTTATATAT CGGTTTTTCC CCTTATATAT CGGTTTTTCC CCTTATATAT CGGTTTTTTCC CCTTATATAT CGGTTTTTCC CCTTATATAT CGGTTTTTTCC CCTTATATATAT CGGTTTTTCC CCTTATATATAT CGGTTTTTTCC CCTTATATATAT CGGTTTTTTCCTCATC TGGTTTTTTCCTCATC TGGTTTTTTCCTCATC TGTTTTTCCTCATC TGTTTTTTTTTT	Ser Asn Thr Ala Leu Arg 1040  CTT TCA CAT GTC GTG TCG Leu Ser His Val Val Ser 1055  AGC AAA GGG TGC AGC AGC Ser Lys Gly Cys Ser Ser 1070  CTC TCC AAA GCT TAA TCAC Leu Ser Lys Ala End 1085  GGTTTCA TCTTATATGA TTATAT GGTAAGT CAGTCCCATA ATAATAT AGTTGGT TCAGTAGTGA TTAGTC GCTGTTA ACTAGTGGTA ATATC TAGTATG GAAATGAATT GCTAGC TTATTTC TTTCCTCATC TCATGT	Ser Asn Thr Ala Leu Arg Ser  1040  CTT TCA CAT GTC GTG TCG CTT Leu Ser His Val Val Ser Leu 1055  AGC AAA GGG TGC AGC AGC TCC Ser Lys Gly Cys Ser Ser Ser 1070  CTC TCC AAA GCT TAA TCAGATAT Leu Ser Lys Ala End 1085  GGTAAGT CAGTCCCATA ATAATAATGT GGTAAGT TCAGTAGTGA TTAGTCTCAT GCTGTTA ACTAGTGGTA ATATCATAGGTGTA ACTAGTGGTA ATATCTAAGGTGTATTCTCTCATC TCATGTAAAAT TTATTTC TTTCCTCATC TCATGTAAAATTTTTTTTCC CCTTATATAT CTGTATTATT	Ser Asn Thr Ala Leu Arg Ser Leu  1040  CTT TCA CAT GTC GTG TCG CTT GAC Leu Ser His Val Val Ser Leu Asp 1055  AGC AAA GGG TGC AGC AGC TCC GAG Ser Lys Gly Cys Ser Ser Ser Glu 1070  CTC TCC AAA GCT TAA TCAGATATCT C Leu Ser Lys Ala End 1085  GGTATCA TCTTATATGA TTATATCATA AGA AGTTGGT TCAGTAGTGA TTAGTCTCAT AAA GCTGTTA ACTAGTGGTA ATATCTAAGC TCA GCTGTTA ACTAGTGGTA ATATCTAAGC TCATCTATCT GAAATTCTC TTATCTCATC TCATGTAAAA ACA CTTTTTCC CCTTATATAT CTGTATTATT TCATCTTTTCC CCTTATATAT CTGTATTATT TCATCTTTTTCC CCTTATATAT CTGTATTATT TCATCTTTTTTCC CCTTATATATT CTGTATTATT TCATCTTTTTTTTTT	Ser Asn Thr Ala Leu Arg Ser Leu His 1040  CTT TCA CAT GTC GTG TCG CTT GAC AGC Leu Ser His Val Val Ser Leu Asp Ser 1055  AGC AAA GGG TGC AGC AGC TCC GAG ATC Ser Lys Gly Cys Ser Ser Ser Glu Ile 1070  CTC TCC AAA GCT TAA TCAGATATCT GCTGG Leu Ser Lys Ala End 1085  GGTAAGT CAGTCCCATA ATAATAATGT ACTTCAG AGTTGGT TCAGTAGTGA TTAGTCTCAT AATAATG GCTGTTA ACTAGTGGTA ATATCTAAGC TCAACAA TAGTATG GAAATGAATT GCTAGCTGTT GATCTC TTATTTC TTTCCTCATC TCATGTAAAA ACAATT	Ser Asn Thr Ala Leu Arg Ser Leu His Ala  1040  CTT TCA CAT GTC GTG TCG CTT GAC AGC CCC Leu Ser His Val Val Ser Leu Asp Ser Pro-  1055  AGC AAA GGG TGC AGC AGC TCC GAG ATC CAG Ser Lys Gly Cys Ser Ser Ser Glu Ile Gln  1070  CTC TCC AAA GCT TAA TCAGATATCT GCTGCTTTC Leu Ser Lys Ala End  1085  GGTTTCA TCTTATATGA TTATATCATA AGATACTATA  GGTAAGT CAGTCCCATA ATAATAATGT ACTTCAGAAC  AGTTGGT TCAGTAGTGA TTAGTCTCAT AATAATCATA  GCTGTTA ACTAGTGGTA ATATCTAAGC TCAACAATAA  PAGTATG GAAATGAATT GCTAGCTGTT GATCTCTTTC  TTATTTC TTTCCTCATC TCATGTAAAA ACAATTTTCT	Ser Asn Thr Ala Leu Arg Ser Leu His Ala Asn 1040 1045  CTT TCA CAT GTC GTG TCG CTT GAC AGC CCC AAT Leu Ser His Val Val Ser Leu Asp Ser Pro Asn 1055 1060  AGC AAA GGG TGC AGC AGC TCC GAG ATC CAG TCC Ser Lys Gly Cys Ser Ser Ser Glu Ile Gln Ser 1070 1075  CTC TCC AAA GCT TAA TCAGATATCT GCTGCTTTCT TC Leu Ser Lys Ala End 1085  GGTTTCA TCTTATATGA TTATATCATA AGATACTATA TAAC GGTAAGT CAGTCCCATA ATAATAATGT ACTTCAGAAC CACA AGTTGGT TCAGTAGTGA TTAGTCTCAT AATAATCATA TAAC GCTGTTA ACTAGTGGTA ATATCTAAGC TCAACAATAA AGAC PAGTATG GAAATGAATT GCTAGCTGTT GATCTCTTC CCTC TTATTTC TTTCCTCATC TCATGTAAAA ACAATTTTCT GAAC PTTTTTCC CCTTATATAT CTGTATTATT TCTACTATTT TTTC	Ser Asn Thr Ala Leu Arg Ser Leu His Ala Asn Arg 1040 1045  CTT TCA CAT GTC GTG TCG CTT GAC AGC CCC AAT ATT Leu Ser His Val Val Ser Leu Asp Ser Pro Asn Ile 1055 1060  AGC AAA GGG TGC AGC AGC TCC GAG ATC CAG TCC ATC Ser Lys Gly Cys Ser Ser Ser Glu Ile Gln Ser Ile 1070 1075  CTC TCC AAA GCT TAA TCAGATATCT GCTGCTTTCT TTTGGG Leu Ser Lys Ala End 1085  GGTAAGT CAGTCCCATA ATAATAATGT ACTTCAGAAC CACAATAG AGTTGGT TCAGTAGTGA TTAGTCTCAT AATAATCATA TAATTACC GCTGTTA ACTAGTGGTA ATATCTAAGC TCAACAATAA AGATGTA PAGTATG GAAATGAATT GCTAGCTGTT GATCTCTTC CCTTTAT  TTATTTC TTTCCTCATC TCATGTAAAA ACAATTTTCT GAAGGTG	Ser Asn Thr Ala Leu Arg Ser Leu His Ala Asn Arg Ser  1040 1045 1  CTT TCA CAT GTC GTG TCG CTT GAC AGC CCC AAT ATT GGC Leu Ser His Val Val Ser Leu Asp Ser Pro Asn Ile Gly 1055 1060 1  AGC AAA GGG TGC AGC AGC TCC GAG ATC CAG TCC ATC GTC Ser Lys Gly Cys Ser Ser Ser Glu Ile Gln Ser Ile Val 1070 1075 1  CTC TCC AAA GCT TAA TCAGATATCT GCTGCTTTCT TTTGGGTAA Leu Ser Lys Ala End 1085  GGTTTCA TCTTATATGA TTATATCATA AGATACTATA TAAGCACCTT  GGTAAGT CAGTCCCATA ATAATAATGT ACTTCAGAAC CACAATACTT  AGTTGGT TCAGTAGTGA TTAGTCTCAT AATAATCATA TAATTACACA GCTGTTA ACTAGTGGTA ATATCTAAGC TCAACAATAA AGATGTAAAA	CTT TCA CAT GTC GTG TCG CTT GAC AGC CCC AAT ATT GGC GAG  Leu Ser His Val Val Ser Leu Asp Ser Pro Asn Ile Gly Glu  1055  AGC AAA GGG TGC AGC AGC TCC GAG ATC CAG TCC ATC GTC ACA  Ser Lys Gly Cys Ser Ser Ser Glu Ile Gln Ser Ile Val Thr  1070  1075  CTC TCC AAA GCT TAA TCAGATATCT GCTGCTTTCT TTTGGGTAAG  Leu Ser Lys Ala End  1085  GGTTTCA TCTTATATGA TTATATCATA AGATACTATA TAAGCACCTT  GGTAAGT CAGTCCCATA ATAATAATGT ACTTCAGAAC CACAATACTT  AGTTGGT TCAGTAGTGA TTAGTCTCAT AATAATCATA TAATTACACA  GCTGTTA ACTAGTGGTA ATATCTAAGC TCAACAATAA AGATGTAAAA  PAGTATG GAAATGAATT GCTAGCTGTT GATCTCTTC CCTTTATTCT  TTATTTC TTTCCTCATC TCATGTAAAA ACAATTTTCT GAAGGTGTAC

65

## ATAAAGCTTA TTCGAGTTAA AAAAAAAAA AAAAAAAA

3635

4. DNA sequence with the coding region for sucrose-synthase for the preparation of sugar beet with modified sucrose concentration, characterised in that the sequence has the following nucleotide sequence (Seq. ID No.4):

CT GCA GGA GGG AAA CAA ATT CTT AGC GAT GGC CCG TTT AGC GAA 0044
Ala Gly Gly Lys Gln Ile Leu Ser Asp Gly Pro Phe Ser Glu
5 10

GTT CTT AGG TCT GCT CAG GAA GCA ATA GTT GTT CCT CCC TTT GTT 0089
Val Leu Arg Ser Ala Gln Glu Ala Ile Val Val Pro Pro Phe Val

15 20 25

GCT ATA GCA GTC CGT CCA AGA CCT GGA GTT TGG GAA TAT GTT CGT 0134
Ala Ile Ala Val Arg Pro Arg Pro Gly Val Trp Glu Tyr Val Arg
30 35 40

GTT AAT GTC TCT GAA CTG AAT GTG GAG CAG CTA ACT GTG TCT GAG 0179
Val Asn Val Ser Glu Leu Asn Val Glu Gln Leu Thr Val Ser Glu
45 50 55

TAT CTC CAT TTC AAG GAA GAA CTT GTG GAT GGA AAG GCT GAT GAC 0224

Tyr Leu His Phe Lys Glu Glu Leu Val Asp Gly Lys Ala Asp Asp
60 65 70

CAC TAT GTG CTT GAG CTT GAT TTC GAG CCT TTT AAT GAA TCA GTT 0269

His Tyr Val Leu Glu Leu Asp Phe Glu Pro Phe Asn Glu Ser Val

75 80 85

CCA CGT CCA ACT CGC TCT TCA TCA ATT GGT AAT GGT GTT CAG TTC 0314

Pro Arg Pro Thr Arg Ser Ser Ile Gly Asn Gly Val Gln Phe
90 95 100

CTC AA Leu As 105							0359
TTG GA Leu Gl 120							0404
GTT GT Val Va 135							0449
CAG TO Gln Se 150							0494
GCA GA Ala As 165							0539
GGT TT Gly Ph 180							0584
ATG AT Met Me							0629

	······	ACA	TTA	GAG	ACA	ттт	CTG	GGA	AGA	CTT	ccc	ATG	GTG	TTT	AAT	GTG	0674
,	1	Thr	Leu	Glu	Thr	Phe	Leu	Gly	Arg	Leu	Pro	Met	Val	Phe	Asn	Val	
		210					215					220					
٠																	
	1	GTC	ATT	TTG	TCT	GTA	CAT	GGA	TAT	TTT	GGA	CAG	GCA	CAT	GTG	CTC	0719
	•	Val	Ile	Leu	Ser	Val	His	Gly	Tyr	Phe	Gly.	_Gln-	Ala	His	Val	Leu	
		225					230					235					
																	•
												TAT.					0764
	(	Gly	Leu	Pro	Asp	Thr	Gly	Gly	Gln	Ile	Val	Tyr	Ile	Leu	Asp	Gln	
		240					245					250					
												CGA					0809
			Arg	Ser	Leu	Glu		GIU	Met	Leu	GIn	Arg	116	гуs	rys	GIN	
		255					260					265					
		CCA	СТА	СУТ	GTG	<b>ል</b> ርጥ	ССТ	AGA	ልጥጥ	СФФ	АТС	GTG	A'GT	·cgg	TTG	ATT	0854
												Val					
		270	Dea	nop	•	****	275	•••				280		9			
		270					2.3										
		CCT	GAC	GCT	AAA	GGG	ACC	ACG	TGC	AAT	CAA	CGT	ATG	GAG	AAA	GTC	0899
												Arg					
		285	-		_	_	290					295					
											•						
•																	
		AGT	GGA	ACA	GAG	CAT	GCT	AGT	ATC	CTG	AGA	GTT	CCT	TTC	CGA	TCA	0944
•		Ser	Gly	Thr	Glu	His	Ala	Ser	Ile	Leu	Arg	Val	Pro	Phe	Arg	Ser	
		300		•			305					310					

CNC	* * *	GGA	ATC	СТС	CGC	AAA	TGG	ATA	TCT	AGA	TTT	GAT	GTA	TGG	0989	
			Ile													,
	гуѕ	GIY	116	Dea	320	ביים			001	325	• • • • • • • • • • • • • • • • • • • •	<b>-</b>		. •		
315					320					323						٠.
					2-									3 MM	1004	
														ATT	1034	
Pro	Tyr	Leu	Glu	Thr	Phe	Thr	Glu	Asp	Ala		Gly	Glu	Ile	Ile		
330					335					340						
GGC	GAG	TTG	CAG	GGT	CGT	CCA	GAT	CTG	ATA	ATT	GGC	AAC	TAC	AGC	1079	
Gly	Glu	Leu	Gln	Gly	Arg	Pro	Asp	Leu	Ile	Ile	Gly	Asn	Tyr	Ser		
345					350					355						
• • •																
CAT	ccc	ייממ	ΔΤΔ	GTT	GCT	тст	TTA	TTG	TCC	CAC	AAA	ATG	GGT	GTC	1124	
			Ile													
360	GIY	no	110	,,,	365					370	•		•			
360					303											
				3.07.3	CCC	CAT	CCA	ጥጥር	G J G	אאא	A C C	AAG	ጥልጥ	CCA	1169	
	Gln	Cys	Asn	TIE		Mis	Ala	Leu	GIU		1111	пλэ	ıyı	FIO		
375					380					385						
			ATT												1214	
Asp	Ser	Asp	Ile	Tyr	Trp	Lys	Arg	Phe	Glu	Asp	Lys	Tyr	His	Phe		
390					395					400	•					
																*
					•	•										
TCG	TGT	CAA	TTT	TCA	GCT	GAC	TTG	ATG	GCA	ATG	AAT	CAT	GCT	GAT	1259	,
														Asp		
405	- 1 -				410					415						

TTC	ATC	ATT	ACG	AGT	ACT	TAC	CAA	GAG	ATA	GCT	GGA	ACG	AAG	AAT	1304
Phe	Ile	Ile	Thr	Ser	Thr	Tyr	Gln	Glu	Ile	Ala	Gly	Thr	Lys	Asn	
420					425					430					
															•
			CAA												1349
	val	GIĀ	Gln	Tyr	440	Ser	пте	гÃг	Ald	445	THE	Pne	PIO	GIY	
435					440					443					
CTG	TAT	CGG	GTG	GTT	CAC	GGG	ATT	GAT	GTC	TTT	GAT	ccc	AAG	TTT	1394
			Val												
450	•	_			455					460					
								•							
									•						
TAA	ATT	GTC	TCG	CCA	GGG	GCA	GAC	ATG	GCC	ATC	TAC	TTC	CCA	TTT	1439
Asn	Ile	Val	Ser	Pro	Gly	Ala	Asp	Met	Ala	Ile	Tyr	Phe	Pro	Phe	
465					470					475					
ma »	CAC	220	GAT	CTTC	200	ጥርጥ	CTIC	እ ርጥ	TC N	CTTT	C N TT	202	CTTT	א ידי א	1484
			Asp										2		1404
480	GIU	гус	ASP	Vai	485	Cys	рец	****	Jei	490	1113	nr 9	Бец	110	
400					403					450					
GAG	CAG	CTC	CTA	TTC	AAA	CCT	GAG	CAG	AAC	GAA	GAA	CAC	ATT	GGT	1529
Glu	Gln	Leu	Leu	Phe	Lys	Pro	Glu	Gln	Asn	Glu	Glu	His	Ile	Gly	
495					500					505					
						•									
														AGG	1574
Val	Leu	Asp	Asp	Thr	Ser	Lys	Pro	Ile	Ile	Phe	Ser	Met	Ala	Arq	
510					515					520					

CTA	GAC	CGT	GTG	AAG	AAT	ATA	ACA	GGG	CTG	GTA	GAG	TGC	TAT	GGC	1619	
Leu	Asp	Arg	Val	Lys	Asn	Ile	Thr	Gly	Leu	Val	Glu	Cys	Tyr	Gly		
525					530					535						
AAG	AAT	GCG	AAA	CTC	AGG	GAA	CTG	GCA	AAC	CTG	GTT	GTA	GTG	GCT	1664	
_										Leu						
540			-1-		545					550						
340																
666	m» c	አአጥ	C አጥ	CT A	מממ	AAG	ጥርር	ልልጥ	GAC	AGG	GAG	GAA	АТТ	GCC	1709	
										Arg						
-	TYL	ASII	ASP	Vai	560	DyS	Der	NO.II	usb	565	014	014				
555					560					505						
				<b>.</b>	<b>63.6</b>	200	C.M.M.	3 (11) 3	CAC	CAC	m v m	יחממ	ע יחיים	A C A	1754	
										GAG					1/34	-
	Ile	Glu	Lys	Met		Arg	Leu	TIE	GIN	Glu	Tyr	ASII	Leu	AIG		
570					575					580						
												am s	663	3 3 C	1700	
														AAT	1799	
Gly	Gln	Phe	Arg	Trp		Ala	Ser	Gln	Thr	Asn	Arg	vaı	Arg	ASN		
585					590					595						
						•										
										GGA					1844	
Gly	Glu	Leu	Tyr	Arg	Tyr	Ile	Cys	Asp	Lys	Gly	Gly	Ile	Phe	Ala		
600					605					610						
																•
														GCC	1889	J
Gln	Pro	Ala	Phe	Tyr	Glu	Ala	Phe	Gly	Leu	Thr	Val	Val.	Glu	Ala		
615					620					625						

					TGC Cys 640			1934
					TTT Phe 655		CCA Pro	1979
					GAA Glu 670			2024
				Lys	ATC Ile 685			2069
				Trp	CAA Gln 700			2114
				Gly	TTC Phe 715			2159
				Arg	TAT Tyr 730		TTC Phe	2204

TAC	ATT	TTG	AAG	TTC	CGT	GAT	CTG	GCC	AAC	TCT	GTT	CCG	CTG	GCA	2249
Tyr	Ile	Leu	Lys	Phe	Arg	Asp	Leu	Ala	Asn	Ser	Val	Pro	Leu	Ala	
735					740					745					
														CGT	2294
Thr	Asp	Glu	Glu	Pro	Ser	Thr	Thr	Asp	Ala	Val	Ala	Thr	Phe	Arg	
750					755					760					
GGA	CCT	TGA	ACG	CTGCT	rgc 1	TACI	rgago	T TO	CAAC	GTTGT	r GT?	ATATA	ATTA		2343
Gly	Pro	End													
						-m. c.			ammon		OM 3 (1	nm > < n	n % m		2393
CTGT	'GAAA	IGG A	ATAA	AGT G	ra Go	JIACA	ACAAA	A AGC	311C	ICAA	CIAI	L'IMG1	LAI		2393
omm <i>c</i>	meme	ישר ח	[AAA]	רא א <i>ר</i> יכ	7 N G 7	\стс!	1 A A A A	י שכיי	יי <b>ר</b> מיח	ייייכ	ጥጥር፣	י תיכינים (	ماسات		2443
CTTC	.1010	,16	LAAA	IMACC	JA GI	1010	uuuu	. 101	INNII	1110	IIGr	11010	- + +		2413
GAAR	ል ሮሞር	: AG 5	rttgo	ייייייי	ኃጥ ጥባ	ראידים	ርጥጥ A <i>E</i>	GTC	TATO	GACA	ATAT	rgtai	rca		2493
GAAL	WOIG	, no									••••				
ጥልጥዶ	ACGO	AT 1	CTTC	CAGTO	SA TO	CATAT	CAA	A A A	TACI	rgac	CATO	CGAAC	STT		2543
AATO	AAA	TC (	SACAC	CAAC	CA										2563
	<del>-</del>														
	5.	E	eriv	ativ	es c	of DN	IA se	quen	ces	acco	rdin	g to	any	one	of
		_	. 1	1	+-	4 01		+~~i	c 0 đ	in +	hat	thec			

- 5. Derivatives of DNA sequences according to any one of claims 1 to 4 characterised in that these derivatives are obtained by exchange of single bases or by targeted or non-targeted mutagenesis.
- 6. Plasmids containing

5

a) a suitable promoter which ensures that the coding sequence meets a suitable time point or in the specified developments in the transgenic plant or in determined genes of transgenic plants;

5

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- at least one coding sequence according to claims 1 to 5, thati) is so coupled to the promoter that the
  - i) is so coupled to the promoter that the formation of an RNA is allowed which is into a protein, whereby the protein demonstrates an enzymatic activity which leads to a modification of the sucrose concentration in the plant, or
  - ii) which is so coupled to the promoter that the coding part is read, which leads to the formation of a so-called anti-sense RNA which under-expresses the formation of the protein coded from an endogenous gene in the plant, that is involved in the sucrose biosynthesis; and
- c) A non-coding termination sequence that contains the signal for the termination and polyadenylation of the transcript.
- Use of the DNA-sequences according to any one of claims 1 to 6 for the preparation of sugar beet with changed sucrose concentration.
- 25 8. Use of the plasmids according to any one of claims 1-4 for the preparation of derivatives by targeted or non-targeted mutagenesis
- 9. Sugar beet containing a DNA sequence according to any one of claims 1-5.